BEST AVAILABLE COPY

Access DB# 11184()

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Maur Art Unit: \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	on: <u>(2 annsen</u>	Results Format Pre	ferred (circle): PAP	: <u> - </u>
Please provide a detailed statement of the Include the elected species or structures utility of the invention. Define any term known. Please attach a copy of the covered to the covered t	e search topic, and des keywords, synonyms, is that may have a spec r sheet, pertinent claim	**************** cribe as specifically as p acronyms, and registry ial meaning. Give exan s, and abstract.	*************** rossible the subject ma numbers, and combine raples or relevant citation	with the concept or ons, authors, etc, if
Title of Invention: And -Los Inventors (please provide full names):	le Isotope hass spectron	-Coded Extra	actiont (ALIC Sis of Protei	5) VIIIS Use a monthes
Dong Chang Quu Earliest Priority Filing Date:	Oct. 22, 30	<u> </u>	200 p 200 p 200 pp. (200 pp. (
For Sequence Searches Only Please inc appropriate serial number.	uae au perunent injormi	auon (pareni, cnua, uivisi	onai, or issuea patent nu	mbers) along wan ine
		compound		
Specific	reactive	guoup att	uched to	4 N2n-
July 1 Spolyric	eg bajdw	C : U.U. 4	linker _	Specifically,
the co	angounds :	r futed in	(Paims)	0,13413
Non. In ol	yked poly	mer can b	e polystyr polyetlyle	ne or july
See hig	Lighted	areasinos	claims.	
			D. ,	nks [
Closest art is printed actual abstracts he	cut first ?	don't pavie	, not that,	manij
STAFF USE ONLY	Type of Search	5 S S S S S S S S S S S S S S S S S S S	ors and cost where a	pplicable
Searcher Phone #:	NA Sequence (#) AA Sequence (#)	STN T	1 (
Searcher Location:	Structure (#) /	(う) (Aulika Tara) Questel/Orbit		
Date Searcher Picked Up:	Bibliographic /	Dr.Link		
Date Completed: 1 (2)	Litigation	Lexis/Nexis	3	
Clerical Prep Time:	Patent Family	WWW/Internet		

=> file reg FILE 'REGISTRY' ENTERED AT 12:36:39 ON 13 JAN 2004 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2004 American Chemical Society (ACS)

=> display history full 11-

L1	FILE 'LCA' 19434	ENTERED AT 09:39:10 ON 13 JAN 2004 SEA (DETECT? OR SENSE# OR SENSING# OR ANALY? OR ANAL# OR ASSAY? OR EST# OR ESTN# OR ESTIMAT? OR QUANTIF? OR
		QUANTITAT? OR CALCULAT? OR CALC# OR CALCN# OR MEASUR? OR MONITOR?)/BI,AB
L2	3688	SEA (DETECTOR? OR COUNTER? OR SENSOR? OR SPECTROG? OR SPECTROMET? OR PYROMET? OR METER# OR METRE# OR GAUGE? OR INDICATOR? OR RECORDER? OR ANALYZER? OR SCANNER? OR
		COMPARATOR? OR INSPECTOR? OR MONITOR?)/BI,AB
Г 3	19714	SEA (DETERMIN? OR DETERMN# OR DET# OR DETN# OR EVALUAT? OR ASCERTAIN? OR RECOGNI? OR IDENTIF? OR INDICAT? OR
		DISTINGUISH? OR TEST OR TESTS OR TESTED OR TESTING# OR
		DIAGNOS?)/BI,AB
	FILE 'HCA'	ENTERED AT 09:47:38 ON 13 JAN 2004
L4	208483	SEA (L1 OR L2 OR L3) (2A) PROTEIN?
L5		SEA PEPTIDE# OR DIPEPTIDE# OR TRIPEPTIDE# OR TETRAPEPTIDE # OR PENTAPEPTIDE# OR POLYPEPTIDE#
L6	102329	SEA ?DISULFID? OR ?DISULPHID?
L7	3921	SEA (BLOCK? OR ENDCAP? OR CAP OR CAPS OR CAPPED OR CAPPING# OR TERMINAT?) (2A) (REAG!NT? OR REACTANT? OR COMPOUND# OR CMPD# OR CPD#)
L8	211541	SEA DIGEST?
L9	535848	SEA ISOTOP? OR RADIOISOTOP? OR RADIOLABEL? OR RADIOACTIV? OR RADIO?(2A)(TAG OR TAGS OR TAGGED OR TAGGING# OR LABEL? OR MARK? OR PROBE# OR PROBING#)
	FILE 'REGI	STRY' ENTERED AT 09:52:13 ON 13 JAN 2004 E DEUTERIUM/CN
L10	1	SEA DEUTERIUM/CN
L11		·
L12	FILE 'HCA'	ENTERED AT 09:52:54 ON 13 JAN 2004
L13	145585 122458	SEA L10 OR DEUTERAT? OR DEUTERIUM# OR D2 SEA L11 SEA HPLCMS OR MS OR M(W)S OR MASS##(2A)SPEC?

FILE 'LREGISTRY' ENTERED AT 09:55:05 ON 13 JAN 2004

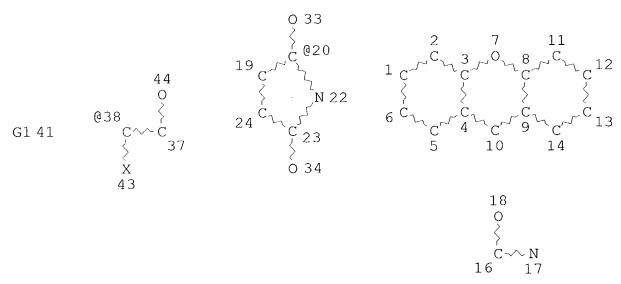
```
STR
L15
    FILE 'REGISTRY' ENTERED AT 10:38:01 ON 13 JAN 2004
               E CYSTEINE/CN
              2 SEA CYSTEINE/CN
L16
    FILE 'HCA' ENTERED AT 10:39:47 ON 13 JAN 2004
     105507 SEA L16 OR ?CYSTEINE?
L17
            319 SEA L4 AND L5 AND (L6 OR SS OR S(W)S) AND L17
L18
              0 SEA L18 AND L7
L19
             65 SEA L18 AND L8
L20
             22 SEA L18 AND L9
L21
             72 SEA L18 AND L14
L22
              5 SEA L18 AND (L12 OR L13)
L23
                D L23 1-5 AU
                SEL L23 2,3 RN
    FILE 'REGISTRY' ENTERED AT 10:47:28 ON 13 JAN 2004
             53 SEA (435314-09-3/BI OR 435314-15-1/BI OR 435314-17-3/BI
1.24
              2 SEA L24 AND L11
L25
              1 SEA 436144-22-8/BI
L26
    FILE 'HCA' ENTERED AT 11:01:26 ON 13 JAN 2004
             1 SEA L26
L27
             10 SEA L20 AND L21
L28
             29 SEA L20 AND L22
L29
             7 SEA L21 AND L22
L30
    FILE 'REGISTRY' ENTERED AT 11:04:55 ON 13 JAN 2004
      114427 SEA L11 AND C/ELS
L31
     FILE 'HCA' ENTERED AT 11:06:55 ON 13 JAN 2004
      54928 SEA L31
L32
           128 SEA L4 AND L32
L33
     FILE 'REGISTRY' ENTERED AT 11:08:29 ON 13 JAN 2004
                E POLYSTYRENE/CN
               1 SEA POLYSTYRENE/CN
L34
                ACT EOEGPOPG/A
                _____
          9682) SEA 75-21-8/CRN
L35 (
L35 ( 9682) SEA 75-21-8/CRN
L36 ( 21863) SEA 107-21-1/CRN
         9283) SEA 75-56-9/CRN
L37 (
L38 ( 8413) SEA 57-55-6/CRN
L39 ( 7690) SEA (L35 OR L36) AND (L37 OR L38)
L40 11 SEA L39 AND 2/NC
```

L41	FILE 'HCA' 330322	ENTERED AT 11:09:25 ON 13 JAN 2004 SEA L34 OR POLYSTYRENE# OR STYRENE#
L42	FILE 'LCA' 320	ENTERED AT 11:09:39 ON 13 JAN 2004 SEA (POLYGLYCOL# OR (POLYALKYLENE# OR POLYETHYLENE# OR POLYPROPYLENE# OR POLYBUTYLENE# OR POLYISOBUTYLENE#) (2A) (GLYCOL# OR OXIDE#) OR (ETHYLENE# OR PROPYLENE# OR BUTYLENE# OR ISOBUTYLENE#) (2A) (POLYOXIDE# OR POLY(W) OXIDE #)) /BI,AB
L43		SEA (POLYOXYALKYLENE# OR POLYOXYETHYLENE# OR POLYOXYPROPY LENE# OR POLYOXYBUTYLENE# OR POLYOXYISOBUTYLENE# OR POLY(W)(GLYCOL# OR OXYALKYLENE# OR OXYETHYLENE# OR OXYPROPYLENE# OR OXYBUTYLENE# OR OXYISOBUTYLENE#))/BI,AB
L44	63	SEA (POLYOXY(W) (ALKYLENE# OR ETHYLENE# OR PROPYLENE# OR BUTYLENE# OR ISOBUTYLENE#) OR PEG OR PPG OR PBG OR ALCOX# OR BREOX# OR CARBOWAX# OR EMKAPOL# OR LUTROL# OR MACROGOL# OR PEO OR PLURACOL# OR PLURIOL# OR POLIKOL# OR
L45	7	POLYOX#)/BI,AB SEA (SUPEROX# OR TENZILIN# OR ADEKA# OR ARCOL# OR EXCENOL# OR LAPROL# OR NIAX# OR PROPYLAN# OR SANNIX# OR VORANOL#)/BI,AB
	FILE 'HCA'	ENTERED AT 11:14:17 ON 13 JAN 2004
L46		SEA L40 OR PEG OR L42 OR L43 OR L44 OR L45
L47		SEA L33 AND L41
L48		SEA L33 AND L46 SEA L48 AND ((L5 OR L6 OR L7 OR L8 OR L9) OR L12 OR L13
L49	19	OR L32 OR L14 OR L17)
L50	10	SEA L28 AND (L20 OR L21 OR L22)
L51		SEA L29 AND L21
L52	FILE 'REGI	STRY' ENTERED AT 11:25:03 ON 13 JAN 2004 STR
L52	50	SEA SSS SAM L52
1100		E 2508.150.23/RID
L54	16305	SEA 2508.150.23/RID
L55	49	SEA L54 AND L11
L56 L57 L58 L59 L60 L61 L62	8278 38 1 1 44 5	ENTERED AT 11:30:01 ON 13 JAN 2004 SEA L54 SEA L55 SEA L57 AND L4 SEA L57 AND ?PROTEIN? SEA L56 AND L4 SEA L60 AND (L6 OR L17) SEA L60 AND (L5 OR L7 OR L8 OR L9 OR L12 OR L32 OR L14
		OR L41 OR L46)

```
15 SEA L62 AND L5
L63
             O SEA L62 AND L7
L64
             3 SEA L62 AND L8
L65
           4 SEA L62 AND L9
2 SEA L62 AND L12
1 SEA L62 AND L32
6 SEA L60 AND L14
L66
L67
L68
L69
            2 SEA L60 AND L41
L70
             3 SEA L60 AND L46
L71
            11 SEA (L65 OR L66 OR L67 OR L68 OR L69 OR L70 OR L71)
L72
             1 SEA L63 AND (L20 OR L21 OR L22 OR L29 OR L49)
L73
     FILE 'REGISTRY' ENTERED AT 11:45:12 ON 13 JAN 2004
             10 SEA SSS SAM L15
L74
L75
                STR L15
             23 SEA SSS SAM L75
L76
            421 SEA SSS FUL L75
L77
                SAV L77 WAL170/A
     FILE 'HCA' ENTERED AT 11:52:07 ON 13 JAN 2004
            197 SEA L77
L78
L79
             87 SEA L78 AND ?PROTEIN?
             21 SEA L79 AND L4
L80
             48 SEA L79 AND L5
L81
            18 SEA L79 AND (L6 OR L17)
L82
            0 SEA L79 AND L7
L83
             3 SEA L79 AND L8
L84
             8 SEA L79 AND L9
L85
            1 SEA L79 AND (L12 OR L32)
5 SEA L79 AND L14
L86
L87
           13 SEA L79 AND L17
L88
            2 SEA L79 AND L41
L89
            3 SEA L79 AND L46
1 SEA L79 AND L57
L90
L91
            14 SEA L84 OR L85 OR L86 OR L87 OR L89 OR L90 OR L91
L92
L93
           12 SEA L80 AND L81
             7 SEA L80 AND L82
L94
L95
L96
            14 SEA L81 AND L82
             18 SEA L23 OR L27 OR L30 OR L47 OR L51 OR L58 OR L59 OR L61
                OR L73 OR L94
```

FILE 'REGISTRY' ENTERED AT 12:36:39 ON 13 JAN 2004

=> d 177 que stat L75 STR



VAR G1=38/20 NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 29

STEREO ATTRIBUTES: NONE L77 421 SEA FILE=REGISTRY SSS FUL L75

100.0% PROCESSED 6384 ITERATIONS SEARCH TIME: 00.00.01

421 ANSWERS

=> file hca

FILE 'HCA' ENTERED AT 12:37:17 ON 13 JAN 2004

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> d 198 1-28 cbib abs hitstr hitind

L98 ANSWER 1 OF 28 HCA COPYRIGHT 2004 ACS on STN

139:191379 E2 displacement assay for identifying inhibitors of human papillomavirus (HPV). White, Peter; Yoakim, Christiane (Boehringer Ingelheim (Canada) Ltd., Can.). PCT Int. Appl. WO 2003067259 A1 20030814, 56 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-CA155 20030204. PRIORITY: US 2002-PV355711 20020207.

$$\begin{array}{c} \text{Br} \\ \text{Br} \\ \text{Me}_{2}\text{N} \\ \text{CH}_{2}-\text{NH}-\text{CO} \end{array}$$

The invention provides an assay for identifying inhibitors of HPV, comprising: (a) contacting a HPV E2 transactivation domain with a probe to form a E2:probe complex and measuring a signal from the probe to establish a baseline level; (b) incubating the E2:probe complex with a test compd. and measuring the signal from the probe; (c) comparing the signal from step (b) with the signal from step (a). The probe is a heterocyclic spiro compd. (Markush included) or a deriv. thereof, wherein the deriv. includes a detectable label or an affinity tag. The signal is selected from fluorescence, resonance energy transfer, time-resolved fluorescence, radioactivity, fluorescence polarization, change in the intrinsic spectral properties, luminescence, and plasma-resonance. A modulation in the signal is an indication that the test compd.

I

binds to the transactivation domain. Prepn. of probe mols., e.g. I, is described.

IT 579487-93-7

(E2 displacement assay for identifying inhibitors of HPV)

RN 579487-93-7 HCA

CN Xanthylium, 9-[2-carboxy-4-[[[[4-[(3'R,3'aS,6'aR)-3'-(3,4-dibromophenyl)-3'a,4,4',6,6',6'a-hexahydro-2-methyl-4,4',6,6'-tetraoxospiro[5H-cyclopenta[b]thiophene-5,1'-[1H]furo[3,4-c]pyrrol]-5'(3'H)-yl]phenyl]methyl]amino]carbonyl]phenyl]-3,6-bis(dimethylamino)-, inner salt, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A

PAGE 1-B

```
__Br
IC
     ICM G01N033-569
     ICS C07D497-10
CC
     1-5 (Pharmacology)
     Section cross-reference(s): 28
ΙΤ
     Antiviral agents
     Chemiluminescent substances
     Colored materials
    Drug screening
     Epitopes
     Human
     Human papillomavirus
     Human papillomavirus 11
    Human papillomavirus 6
       Protein sequences
     Test kits
        (E2 displacement assay for identifying inhibitors of HPV)
ΙT
        (gene E1; E2 displacement assay for identifying inhibitors of
       HPV)
ΙT
     Proteins
        (gene E2; E2 displacement assay for identifying inhibitors of
       HPV)
ΙT
     58-85-5, Biotin
                      81-88-9 2321-07-5, Fluorescein
                                                          7440-53-1,
    Europium, biological studies 9014-00-0, Luciferase
                                                            10028-17-8,
     Tritium, biological studies 14158-31-7, Iodine-125, biological
              14762-75-5, Carbon-14, biological studies
     studies
                                                         70281-37-7,
     Tetramethylrhodamine 82354-19-6, Texas red 121207-31-6, Bodipy
              165599-63-3, Bodipy FL 579487-93-7
     493/503
                                                    579487-94-8
     579487-95-9
                   579487-96-0
                                 579487-97-1
                                              579487-98-2
                                                             579487-99-3
     579488-00-9
                   579488-01-0
                                 579488-02-1
        (E2 displacement assay for identifying inhibitors of HPV)
ΤT
     581976-50-3
        (unclaimed protein sequence; e2 displacement assay for
        identifying inhibitors of human papillomavirus (HPV))
    ANSWER 2 OF 28 HCA COPYRIGHT 2004 ACS on STN
```

139:97654 Lysine labeling reagent and methods of use. Peters, Eric C.;

Brock, Ansgar; Ericson, Christer (IRM LLC, Bermuda). PCT Int. Appl. WO 2003056299 A2 20030710, 63 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US35581 20021105. PRIORITY: US 2001-PV332988 20011105; US 2002-PV385835 20020603; US 2002-PV410382 20020912.

AB The present invention provides compds. which are useful as multifunctional labels in proteomics studies. The labels of the present invention are both lysine-specific and increase the overall sequence coverage obtained in polypeptide mapping expts., by for example, increasing the ionization efficiencies of lysine-terminated tryptic fragments. In certain aspects, the labels of the present invention can be used to measure differential quantitation, as for example, deuterium(s) can easily be introduced during their synthesis. In one aspect, a C-terminal derivatized lysine biases the fragment ion intensities strongly toward C-terminal fragment ions, resulting in a highly simplified tandem mass spectrum. In further aspects, the no. of lysine residues can be detd. in a polypeptide. 2-Methoxy-4,5-dihydro-1H-imidazole and 2-methoxy-4,5-tetradeutero-1Himidazole were prepd. and used to label the lysine residues in myoglobin. The myoglobin was digested with trypsin and the peptides were analyzed by MALDI mass spectrometry.

IT 52-90-4, L-Cysteine, reactions

(labeling reagent for, for sequential labeling of polypeptides; lysine-contg. peptide labeling reagent and use in proteomics and mass

spectrometry)

RN 52-90-4 HCA

CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT **37164-19-5**, 1,2-Ethane-1,1,2,2-d4-diamine

(lysine-contg. peptide labeling reagent and use in proteomics and mass spectrometry)

RN 37164-19-5 HCA

CN 1,2-Ethane-1,1,2,2-d4-diamine (9CI) (CA INDEX NAME)

 $H_2N-CD_2-CD_2-NH_2$

IT 352431-28-8P, 2-Imidazolidinethione-4,4,5,5-d4 557064-36-5P

(lysine-contg. peptide labeling reagent and use in proteomics and mass spectrometry)

RN 352431-28-8 HCA

CN 2-Imidazolidinethione-4,4,5,5-d4 (9CI) (CA INDEX NAME)

RN 557064-36-5 HCA

CN 1H-Imidazole-4,5-d2, 4,5-dihydro-4,5-d2-2-(methylthio)-, monohydriodide (9CI) (CA INDEX NAME)

• HI

IT 402788-68-5P

(lysine-contg. peptide labeling reagent and use in proteomics and mass spectrometry)

RN 402788-68-5 HCA

CN 1H-Imidazole-4,5-d2, 4,5-dihydro-4,5-d2-2-methoxy- (9CI) (CA INDEX NAME)

```
ΙT
     7782-39-0, Deuterium, properties
        (lysine-labeling reagent contg.; lysine-contg. peptide
        labeling reagent and use in proteomics and mass
        spectrometry)
     7782-39-0
RN
               HCA
     Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME)
CN
D- D
IC
     ICM G01N
     9-14 (Biochemical Methods)
CC
     Section cross-reference(s): 27
     lysine residue labeling reagent proteomics; mass
ST
     spectrometry labeled lysine peptide;
    methoxyimidazole lysine labeling; deuterium
    methoxyimidazole lysine labeling
     Ion cyclotron resonance mass spectrometry
IT
        (Fourier transform; lysine-contg. peptide labeling
        reagent and use in proteomics and mass
        spectrometry)
ΙΤ
     Alcohols, reactions
        (as carboxylic acid-labeling reagent for sequential labeling of
        polypeptides; lysine-contg. peptide labeling
        reagent and use in proteomics and mass
        spectrometry)
ΙT
     Composition
        (detn. of no. of lysine residues in proteins; lysine-contg.
        peptide labeling reagent and use in proteomics and
        mass spectrometry)
ΙT
     Enzymes, uses
        (digesting proteins, in anal. of
        derivatized proteins by mass
        spectroscopy; lysine-contg. peptide labeling
        reagent and use in proteomics and mass
```

(efficiency of modified lysine-contg. polypeptides; lysine-contg. peptide labeling reagent and use in

spectrometry)

Ionization

ΙT

proteomics and mass spectrometry) ΙT Isotopes (in differential quantitation of lysine-contg. polypeptides; lysine-contg. peptide labeling reagent and use in proteomics and mass spectrometry) ΙT Reagents (labeling lysine residues; lysine-contg. peptide labeling reagent and use in proteomics and mass spectrometry) ΙT Myoglobins (labeling of lysine residues in and anal. of; lysine-contg. peptide labeling reagent and use in proteomics and mass spectrometry) ΙΤ Carboxylic acids, reactions (labeling reagent for, for sequential labeling of polypeptides; lysine-contg. peptide labeling reagent and use in proteomics and mass spectrometry) ΙΤ Electrospray ionization mass spectrometry Mass spectrometry Protein sequences (lysine-contg. peptide labeling reagent and use in proteomics and mass spectrometry) ΙT Peptides, biological studies Proteins (lysine-contg.; lysine-contg. peptide labeling reagent and use in proteomics and mass spectrometry) ΙT Proteins (modified, at lysine residues; lysine-contg. peptide labeling reagent and use in proteomics and mass spectrometry) ΤТ Esterification (of carboxylic acids in sequential labeling of polypeptides; lysine-contg. peptide labeling reagent and use in proteomics and mass spectrometry) ΙT Laser ionization mass spectrometry (photodesorption, matrix-assisted; lysine-contg. peptide labeling reagent and use in proteomics and mass spectrometry) ΙT Laser desorption mass spectrometry (photoionization, matrix-assisted; lysine-contg. peptide labeling reagent and use in proteomics and mass spectrometry) ΙΤ Proteome (studies; lysine-contg. peptide labeling reagent and use in proteomics and mass spectrometry)

```
ΙT
     Affinity
        (tags; lysine-contg. peptide labeling reagent and use
        in proteomics and mass spectrometry)
ΙT
     14464-29-0, Acetic acid N-hydroxysuccinimide ester
        (N-termini of tryptic peptides labeling with;
        lysine-contg. peptide labeling reagent and use in
        proteomics and mass spectrometry)
ΙT
     78348-28-4
        (N-terminus of peptide labeling by; lysine-contg.
        peptide labeling reagent and use in proteomics and
        mass spectrometry)
ΙT
     60108-34-1
                 299899-45-9
                                431063-78-4
                                              543706-56-5
                                                             557064-37-6
                   557064-39-8 557064-40-1
     557064-38-7
                                               557064-41-2
                                                             557064-42-3
                               557064-45-6
     557064-43-4
                   557064-44-5
                                               557064-46-7
                                                             557064-47-8
     557064-48-9
                   557064-49-0 557064-50-3
        (amino acid sequence of tryptic peptides of horse
        myoglobin, derivatization and MALDI mass
        spectrometry in relation to; lysine-contq.
        peptide labeling reagent and use in proteomics and
        mass spectrometry)
ΙT
     83404-43-7
                  106021-96-9
                                115918-58-6
                                              145224-99-3
        (amino acid sequence, mass spectrometry after
        lysine labeling of; lysine-contg. peptide labeling
        reagent and use in proteomics and mass
        spectrometry)
ΙΤ
     71977-09-8
        (amino acid sequence, sequential site-selective labeling of;
        lysine-contg. peptide labeling reagent and use in
        proteomics and mass spectrometry)
ΤТ
     52-90-4, L-Cysteine, reactions
                                      74 - 79 - 3
     L-Arginine, reactions
        (labeling reagent for, for sequential labeling of
        polypeptides; lysine-contg. peptide labeling
        reagent and use in proteomics and mass
        spectrometry)
ΙT
     557064-51-4
        (lysine residue of peptide labeling by; lysine-contg.
        peptide labeling reagent and use in proteomics and
        mass spectrometry)
ΙΤ
     56-87-1, L-Lysine, reactions
        (lysine-contg. peptide labeling reagent and use in
        proteomics and mass spectrometry)
ΙΤ
     74-88-4, Iodomethane, reactions 75-15-0, Carbon disulfide
     , reactions 37164-19-5, 1,2-Ethane-1,1,2,2-d4-diamine
     40322-87-0, 2-Methylthio-2-imidazoline hydroiodide
        (lysine-contg. peptide labeling reagent and use in
        proteomics and mass spectrometry)
ΙT
     352431-28-8P, 2-Imidazolidinethione-4,4,5,5-d4
```

557064-36-5P

(lysine-contg. peptide labeling reagent and use in proteomics and mass spectrometry)

IT 402788-68-5P

(lysine-contg. peptide labeling reagent and use in proteomics and mass spectrometry)

IT 7782-39-0, Deuterium, properties

(lysine-labeling reagent contg.; lysine-contg. peptide labeling reagent and use in proteomics and mass spectrometry)

IT 9002-07-7, Trypsin

(lysine-modified myoglobin digestion with; lysine-contg. peptide labeling reagent and use in proteomics and mass spectrometry)

IT 28118-54-9P

(polypeptides labeling with; lysine-contg. peptide labeling reagent and use in proteomics and mass spectrometry)

- L98 ANSWER 3 OF 28 HCA COPYRIGHT 2004 ACS on STN

 138:381146 Methods for the detection, analysis and isolation of nascent proteins by labeling with reporter dyes using an aminoacyl-tRNA charged with a dye-conjugated amino acid.
 Rothschild, Kenneth J.; Gite, Sadanand; Olejnik, Jerzy (Ambergen, Inc., USA). U.S. Pat. Appl. Publ. US 2003092031 A1 20030515, 76 pp., Cont.-in-part of U.S. Ser. No. 49,332. (English). CODEN: USXXCO. APPLICATION: US 2002-174368 20020618. PRIORITY: US 1999-382736 19990825; WO 2000-US23233 20000823; US 2002-49332 20020621.
- AΒ A non-radioactive method of detection and anal. of nascent proteins translated within cellular or cell-free translation systems by labeling the nascent protein with a reporter The core method involves charging a tRNA with an dye is described. amino acid conjugated with a powerful fluorescent, preferably a deriv. of BODIPY (4,4-difluoro-4-bora-3a,4a-diaza-s-indacene). Alternatively, protein synthesis can be monitored by incorporating a dye-binding peptide into a protein. Binding of the dye to the protein, with a change in its spectral properties, can be used to monitor protein synthesis. Nascent proteins contg. these markers can be rapidly and efficiently detected, isolated and analyzed without the handling and disposal problems assocd. with radioactive reagents. Chem. synthesis of misaminoacylated tRNA-Lys by partial degrdn. of the 3'-end and resynthesis is demonstrated. acid was also labeled with a photolabile biotin that allowed rapid recovery of the protein from cell-free translation with immobilized streptavidin. Lower limits of detection were in the range 0.3-10 ng protein.

114616-31-8D, amino acid conjugates 527687-02-1D, amino acid conjugates

(incorporation into nascent **proteins** of; methods for detection, anal. and isolation of nascent **proteins** by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

RN 114616-31-8 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-ar-carboxamide, N-[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]-3',6'-dihydroxy-3-oxo-(9CI) (CA INDEX NAME)

- RN 527687-02-1 HCA
- CN Xanthylium, 9-[2-carboxy-4(or 5)-[[[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]amino]carbonyl]phenyl]-3,6-bis(dimethylamino)-, inner salt (9CI) (CA INDEX NAME)

IC C12Q001-68; C12P019-34

NCL 435006000

CC 6-1 (General Biochemistry)

Section cross-reference(s): 3, 9

ST **protein** nascent detection fluorescent dye incorporation tRNA misaminoacylation

IT tRNA

(aminoacyl, dye-labeled; methods for detection, anal. and isolation of nascent **proteins** by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT Bacteriorhodopsins

(apobacteriorhodopsins, detection of synthesis of; methods for detection, anal. and isolation of nascent **proteins** by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT Proteins

(carbohydrate-binding, detection of synthesis of; methods for detection, anal. and isolation of nascent **proteins** by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT Translation, genetic

(cell-free, detection of nascent **proteins** in; methods for detection, anal. and isolation of nascent **proteins** by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT Translation, genetic

(detection of nascent proteins in; methods for

detection, anal. and isolation of nascent **proteins** by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT Antigens

Cytokines

Enzymes, analysis

Fusion proteins (chimeric proteins)

Hormones, animal, analysis

(detection of synthesis of; methods for detection, anal. and isolation of nascent **proteins** by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT Escherichia coli

(exts., labeling of nascent **proteins** in; methods for detection, anal. and isolation of nascent **proteins** by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT Fluorometry

(for detection of dye-labeling of nascent proteins; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT Wheat

(germ, exts., labeling of nascent proteins in; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT Avidins

(in purifn. of nascent **proteins** labeled with biotin derivs.; methods for detection, anal. and isolation of nascent **proteins** by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT tRNA

(initiator, labeling by misaminoacylation of; methods for detection, anal. and isolation of nascent **proteins** by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT tRNA

(labeling by misaminoacylation of; methods for detection, anal. and isolation of nascent **proteins** by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT Proteins

(lipid-binding, detection of synthesis of; methods for detection, anal. and isolation of nascent **proteins** by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT Animal cell

Pancreas

Reticulocyte

(lysates, protein synthesis in, detection of; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT tRNA

(lysine-specific, labeling by misaminoacylation of; methods for detection, anal. and isolation of nascent **proteins** by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT Proteins

(nucleic acid-binding, detection of synthesis of; methods for detection, anal. and isolation of nascent **proteins** by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT Egg

(oocyte, protein synthesis in, detection of; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT Animal tissue culture

Insecta

(protein synthesis in, detection of; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT Bacteria (Eubacteria)

Human

Parasite

Virus

(proteins of, detection of synthesis of; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT Hemolysins

(.alpha.-, detection of synthesis of; methods for detection, anal. and isolation of nascent **proteins** by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT 524698-42-8

(detection in nascent **proteins** of; methods for detection, anal. and isolation of nascent **proteins** by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

IT 37353-39-2, RNA ligase

(in prepn. misaminoacylated tRNA; methods for detection, anal. and isolation of nascent **proteins** by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated

amino acid)

- 75-77-4, Trimethylsilyl chloride, reactions ΙT (in protection of deoxycytidine; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)
- ΙT 9013-20-1, Streptavidin (in purifn. of nascent proteins labeled with biotin derivs.; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)
- ΙΤ 58-85-5D, Biotin, amino acid conjugates (in purifn. of nascent proteins; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)
- ΙT 2321-07-5D, Fluorescein, amino acid conjugates 16322-19-3D, amino acid conjugates 113721-87-2D, amino acid conjugates 114616-31-8D, amino acid conjugates 117548-22-8D, amino acid conjugates 145195-58-0D, amino acid conjugates 146616-66-2D, BODIPY-FL-SE, amino acid conjugates amino acid conjugates 217190-15-3D, amino acid conjugates 217190-17-5D, BODIPY-FL-SSE, amino acid conjugates 303190-88-7D, amino acid conjugates 335193-70-9D, BODIPY-R6G-SE, amino acid conjugates 527687-02-1D, amino acid conjugates (incorporation into nascent proteins of; methods for detection, anal. and isolation of nascent proteins by

labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

56-87-1D, L-Lysine, dye conjugates 63-68-3D, L-Methionine, dye ITconjugates

(incorporation into proteins of; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

138026-71-8D, BODIPY, derivs., amino acid conjugates 165599-63-3D, ΙT BODIPY-FL, amino acid conjugates (methods for detection, anal. and isolation of nascent

proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)

- ΙT 9001-78-9, Alkaline phosphatase (partial RNA cleavage with, for misaminoacylation; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid)
- ΙT 13444-71-8, Periodic acid (partial RNA cleavage with, for misaminoacylation; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with

dye-conjugated amino acid) ΙT 17776-78-2 (phosphorylation of deoxyribonucleotides using; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid) ΙT 133852-21-8P (prepn. and reactions of, in prepn. misaminoacylated tRNAs; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid) ΙT 208660-68-8P 328387-23-1P 524698-40-6P (prepn. and reactions of; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid) ΙT 87424-19-9P (prepn. and use in tRNA modification of; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid) ΙT 951-77-9, Deoxycytidine (protection and deprotection of; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid) 69304-37-6 ΙT (reactions of in protection of adenosine; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid) ΙΤ 2592-95-2, 1-Hydroxybenzotriazole 56602-33-6, Benzotriazol-1-yloxy tris-(dimethylamino)phosphonium hexafluoro phosphate (reactions of, in charging tRNA with coumarin amini acids; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid) ΙT 80817-46-5 (reactions of, in prepn. dinucleotides; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid) ΙT 60-32-2, 6-Aminocaproic acid 121-44-8, Triethylamine, reactions 1068-90-2, Diethylacetamidomalonate 6851-99-6, 2-Bromo, 2'-nitroacetophenone 35013-72-0 35231-44-8, 4-(Bromomethyl)-7-methoxy coumarin 82911-69-1 524698-41-7 (reactions of; methods for detection, anal. and isolation of nascent proteins by labeling with reporter dyes using aminoacyl-tRNA charged with dye-conjugated amino acid) ΙΤ 526229-19-6 526229-20-9 526229-21-0 526229-22-1 526229-23-2

526229-24-3 526363-81-5

(unclaimed nucleotide sequence; methods for the detection, anal. and isolation of nascent **proteins** by labeling with reporter dyes using an aminoacyl-tRNA charged with a dye-conjugated amino acid)

- IT 64134-30-1 92000-76-5 145646-22-6 205938-74-5 (unclaimed sequence; methods for the detection, anal. and isolation of nascent **proteins** by labeling with reporter dyes using an aminoacyl-tRNA charged with a dye-conjugated amino acid)
- L98 ANSWER 4 OF 28 HCA COPYRIGHT 2004 ACS on STN

 138:164365 Can nuclear localization signals enhance nuclear localization of plasmid DNA?. Nagasaki, Takeshi; Myohoji, Teruhiko; Tachibana, Taro; Futaki, Shiroh; Tamagaki, Seizo (Department of Applied and Bioapplied Chemistry, Graduate School of Engineering, Osaka City University, Osaka, 558-8585, Japan). Bioconjugate Chemistry, 14(2), 282-286 (English) 2003. CODEN: BCCHES. ISSN: 1043-1802. Publisher: American Chemical Society.
- AB Nonviral vectors are safer and more cost-effective than viral vectors but are significantly less efficient, and thus, increasing the efficiency of nonviral vectors remains an important objective. One way to overcome this problem is by stimulating the nuclear localization of exogenous genes. Nuclear localization signals (NLSs) are known to be involved in the active transport of exogenous proteins and probes into the nucleus. However, stimulation of nuclear localization of plasmid DNA has yet to be confirmed completely. In the present study, we prepd. plasmid DNA-NLS peptide conjugates and adjusted spacer length and no. introduced in an attempt to increase transfection efficiency. In comparison to conjugates with unmodified plasmid DNA and short spacers, we found that NLS-plasmid DNA conjugates with covalent bonding by diazo coupling through PEG chain (MW 3400) stimulated complexation with the nuclear transport proteins importin .alpha. and importin .beta.. Evaluation of transfection showed higher expression efficiency with plasmid DNA-NLS peptide conjugates than with unmodified plasmids. However, evaluation of intracellular trafficking after microinjection into the cytoplasm showed plasmid DNA-NLS peptide conjugates only within the cytoplasm; there was no NLS-plasmid stimulation of nuclear localization. Our findings suggest that stimulation of plasmid nuclear localization cannot be achieved merely by changing spacer length or chem. modifying plasmid DNA-NLS peptide conjugates. An addnl. mechanism must be involved. ΙΤ
- RN 486397-36-8 HCA CN L-Cysteinamide, 1-[4-[[3(or 4)-[3,6-bis(dimethylamino)xanthylium-9-

yl]-4(or 3)-carboxybenzoyl]amino]-1-oxobutyl]-L-prolyl-L-lysyl-L-lysyl-L-lysyl-L-arginyl-L-lysyl-L-valyl-L-alpha.-glutamyl-L-alpha.-aspartyl-L-prolyl-L-tyrosyl-S-[1-[6-[[2-(4-aminophenyl)ethyl]amino]-6-oxohexyl]-2,5-dioxo-3-pyrrolidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

$$\begin{array}{c} CH-(CH_{2}) \, _{4}-NH_{2} \\ C=0 \\ NH_{2} \\ CH-Pr-i \\ C=0 \\ NH \\ CH_{2} \\ CH_{2} \\ CH_{2} \\ CH_{2} \\ CH_{2} \\ CH_{3} \\ CH-CH_{2}-CO_{2}H \\ C=0 \\ NH \\ CH-CH_{2}-CO_{2}H \\ CH-CH_{2}-$$

PAGE 4-A

- CC 3-2 (Biochemical Genetics)
 - Section cross-reference(s): 6

IT Proteins

(NLS (nuclear location signal sequence)-contg.; evaluation of nuclear localization of plasmid DNA-nuclear localization signal peptide conjugate)

- IT Polyoxyalkylenes, biological studies
 (PEG spacer; plasmid DNA-nuclear localization signal peptide conjugation via either short or long spacer)
- Molecular association
 (assocn. of plasmid DNA-nuclear localization signal peptide conjugate with nuclear transport proteins importin .alpha. and .beta.)
- IT Proteins
 (karyopherin .alpha.; assocn. of plasmid DNA-nuclear localization signal peptide conjugate with nuclear transport proteins importin .alpha. and .beta.)
- IT 25322-68-3P, Poly(ethylene glycol)

 (PEG spacer; plasmid DNA-nuclear localization signal peptide conjugation via either short or long spacer)
- IT 486397-36-8DP, conjugated to plasmid pGL3 or pGFP (evaluation of nuclear localization of plasmid DNA-nuclear localization signal peptide conjugate)
- L98 ANSWER 5 OF 28 HCA COPYRIGHT 2004 ACS on STN 138:21796 Methods and compositions related to tagging of membrane surface proteins. Alroy, Iris; Moskowitz, Haim; Reiss, Yuval; Shoham, Benjamin A. (Proteologics, Inc., USA). PCT Int. Appl. WO 2002099077 A2 20021212, 99 pp. DESIGNATED STATES: W: AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). PIXXD2. APPLICATION: WO 2002-US18000 20020606. PRIORITY: US 2001-PV296334 20010606.
- AB The invention relates to methods and reagents for selectively labeling membrane surface proteins using a labeling agent. The label may be used to isolate prepns. of membrane surface proteins. Prepns. of membrane surface proteins may be analyzed by a variety of high-throughput techniques to allow rapid profiling of membrane surface protein compn.
- IT 477876-57-6 477876-66-7

 (methods and compns. related to tagging of membrane surface proteins)
- RN 477876-57-6 HCA

CN Pyrano[3,2-g:5,6-g']diquinolin-13-ium, 6-[2-carboxy-3,4,6-trichloro-5-[[2-[[6-[(2,5-dioxo-3-sulfo-1-pyrrolidinyl)oxy]-6-oxohexyl]amino]-2-oxoethyl]thio]phenyl]-1,2,3,4,8,9,10,11-octahydro-2,2,4,8,10,10-hexamethyl-12,14-disulfo-, inner salt (9CI) (CA INDEX NAME)

RN 477876-66-7 HCA

CN Pyrano[3,2-g:5,6-g']diquinolin-13-ium, 6-[2-carboxy-3,4,6-trichloro-5-[[2-[[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]amino]-2-oxoethyl]thio]phenyl]-1,2,3,4,8,9,10,11-octahydro-2,2,4,8,10,10-hexamethyl-12,14-disulfo-, inner salt (9CI) (CA INDEX NAME)

IC ICM C12N

CC 9-14 (Biochemical Methods)

Section cross-reference(s): 6

ST surface protein label tagging proteome sample prepn

IT Gel electrophoresis

(SDS; methods and compns. related to tagging of membrane surface proteins)

ΙΤ Proteins (SU (surface); methods and compns. related to tagging of membrane surface proteins) ΙT Chelating agents (divalent; methods and compns. related to tagging of membrane surface proteins) ΙT Animal cell Disease, animal Disulfide group Eukaryota Fluorescent substances Labels Linking agents Mass spectrometry Organelle Protein motifs Radioactive substances Reduction Sample preparation Virus Washing (methods and compns. related to tagging of membrane surface proteins) ΙT Proteins (methods and compns. related to tagging of membrane surface proteins) Agglutinins and Lectins ΙT (methods and compns. related to tagging of membrane surface proteins) Thiols (organic), properties ΙΤ (methods and compns. related to tagging of membrane surface proteins) Extracellular matrix ΙΤ (removal of; methods and compns. related to tagging of membrane surface **proteins**) ITOrganelle (vesicle; methods and compns. related to tagging of membrane surface **proteins**) 477876-55-4 **477876-57-6** 477876-59-8 477876-62-3 IT477937-32-9 477937-33-0 477876-64**-**5 **477876-66-7** 477937-35-2 477937-36-3 477937-34-1 (methods and compns. related to tagging of membrane surface proteins) ΙT 60-00-4, EDTA, uses (methods and compns. related to tagging of membrane surface

proteins)

L98

ANSWER 6 OF 28 HCA COPYRIGHT 2004 ACS on STN

137:348617 Acid-labile isotope-coded extractants: A Class of reagents for quantitative mass spectrometric analysis of complex protein mixtures. Yongchang; Sousa, Eric A.; Hewick, Rodney M.; Wang, Jack H. (Proteomics/Protein Chemistry Department, Cambridge, MA, 02140, Analytical Chemistry, 74(19), 4969-4979 (English) 2002. CODEN: ANCHAM. ISSN: 0003-2700. Publisher: American Chemical Society. Quant. mass spectrometry using stable isotope-labeled tagging reagents such as isotope -coded affinity tags has emerged as a powerful tool for identification and relative quantitation of proteins in current proteomic studies. Here we describe an integrated approach using both automated two-dimensional liq. chromatog./mass spectrometry (2D-LC/MS) and a novel class of chem. modified resins, termed acid-labile isotope-coded extractants (ALICE), for quant. mass spectrometric anal. of protein mixts. ALICE contains a thiol-reactive group that is used to capture all cysteine (Cys)-contg. peptides from peptide mixts., an acid-labile linker, and a nonbiol. polymer. The acid-labile linker is synthesized in both heavy and light isotope-coded forms and therefore enables the direct relative quantitation of peptides/proteins through mass spectrometric anal. To test the ALICE method for quant. protein anal., two model protein mixts. were fully reduced, alkylated, and digested in soln. sep. and then Cys-contg. peptides covalently captured by either light or heavy ALICE. The reacted light and heavy ALICE were mixed and washed extensively under rigorous conditions and the Cys-contq. peptides retrieved by mild acid-catalyzed elution. Finally, the eluted peptides were directly subjected to automated 2D-LC/ MS for protein identification and LC/ MS for accurate relative quantitation. Our initial study showed that quantitation of protein mixts. using ALICE was accurate. In addn., isolation of Cys-contq. peptides by the ALICE method was robust and specific and thus yielded very low background in mass spectrometric studies. Overall, the use of ALICE provides improved dynamic range and sensitivity for quant. mass spectrometric anal. of peptide or protein mixts. ΙT 436144-21-7P (acid-labile isotope-coded extractants for quant. mass spectrometric anal. of complex protein mixts.) RN 436144-21-7 HCA

1H-Pyrrole-1-hexanamide, 2,5-dihydro-N-(3-hydroxy-9H-xanthen-9-yl)-

2,5-dioxo- (9CI) (CA INDEX NAME)

CN

CC 9-5 (Biochemical Methods)

ST acid labile isotope coded extractant reagent mass spectrometry

IT Mass spectrometry

Process automation

Sample preparation

Simulation and Modeling, physicochemical

(acid-labile isotope-coded extractants for quant.

mass spectrometric anal. of complex
protein mixts.)

IT Peptides, analysis

Proteins

(acid-labile isotope-coded extractants for quant.

 $\ensuremath{\mathtt{mass}}$ spectrometric anal. of $\ensuremath{\mathtt{complex}}$

protein mixts.)

IT Mass spectrometry

(liq. chromatog. combined with; acid-labile isotope

-coded extractants for quant. mass

spectrometric anal. of complex protein

mixts.)

IT Liquid chromatography

(mass spectrometry combined with; acid-labile

isotope-coded extractants for quant. mass

spectrometric anal. of complex protein

mixts.)

IT Albumins, analysis

(serum, bovine; acid-labile isotope-coded extractants

for quant. mass spectrometric anal.

of complex protein mixts.)

IT 436144-21-7P

(acid-labile isotope-coded extractants for quant.

mass spectrometric anal. of complex
protein mixts.)

L98 ANSWER 7 OF 28 HCA COPYRIGHT 2004 ACS on STN

137:306948 Multiplex detection of nucleic acid or protein by

mass spectrometry using a probe with a cleavable
photosensitive or chemi-activatable tag. Matray, Tracy J.;
Hernandez, Vincent S.; Chenna, Ahmed; Hooper, Herbert; Singh, Sharat
(Aclara Biosciences, Inc., USA). U.S. Pat. Appl. Publ. US
2002150927 A1 20021017, 25 pp., Cont.-in-part of U.S. Ser. No.
698,846. (English). CODEN: USXXCO. APPLICATION: US 2001-8593
20011109. PRIORITY: US 1999-303029 19990430; US 2000-561579
20000428; US 2000-602586 20000621; US 2000-684386 20001004; US
2000-698846 20001027.

The invention provides a method for detecting a target analyte, by: AΒ (a) contacting one or more target analytes with a set of first and second binding reagents under conditions sufficient for binding of a target analyte with the first and second binding reagents, each of the first binding reagents contg. a cleavage-inducing moiety and a target binding moiety, each of the second binding reagents contg. a tagged probe having a mass modifier region attached to a target binding moiety by a cleavable linkage, the cleavable linkage being susceptible to cleavage when in proximity to an activated cleavage-inducing moiety; (b) activating the cleavage-inducing moiety to release a tag reporter, and (c) detecting a mass of the tag reporter, the mass uniquely corresponding to a known target analyte. The sequence contg. the SNP is exemplary of DNA sequences of interest generally. Detection of multiple tag reporters using mass spectrometry are described, including synthesis of tag reagents and conjugation of sensitizer mols. to

assay reagents. A sandwich-type immunoassay for six cytokines is carried out for the qualification and quantification of known cytokine antigens. In this assay, a matched pair of antibodies forms a sandwich around a cytokine antigen bringing the two antibodies in close proximity to allow the singlet oxygen cleave the cleavable linkage of the tagged probe.

IT 471244-00-5P 471244-01-6P 471244-02-7P 471244-03-8P 471244-04-9P 471244-05-0P 471244-06-1P 471244-07-2P 471244-08-3P 471244-09-4P

(as cleavable reporter conjugated to probe; methods for detecting a plurality of analytes by mass spectrometry)

RN 471244-00-5 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-5-carboxamide, N-[1-[[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3oxopropyl]thio]acetyl]amino]-1-methylethyl]-3',6'-dihydroxy-3-oxo-(9CI) (CA INDEX NAME)

RN 471244-01-6 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-5-carboxylic acid, 3',6'-dihydroxy-3-oxo-, 2-[[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropyl]thio]acetyl]hydrazide (9CI) (CA INDEX NAME)

RN 471244-02-7 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-5-carboxamide,
N-[8-[[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3oxopropyl]thio]acetyl]amino]octyl]-3',6'-dihydroxy-3-oxo- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 471244-03-8 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-5-carboxamide, N-[13-[(2,5-dioxo-1-pyrrolidinyl)oxy]-8,13-dioxo-2,5-dioxa-10-thia-7-azatridec-1-yl]-3',6'-dihydroxy-3-oxo-(9CI) (CA INDEX NAME)

PAGE 1-À

PAGE 1-B

RN 471244-04-9 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-5-carboxamide, N-[18-[(2,5-dioxo-1-pyrrolidinyl)oxy]-13,18-dioxo-3,6,9-trioxa-15-thia-12-azaoctadec-1-yl]-3',6'-dihydroxy-3-oxo-(9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

$$- CH_2 - O - CH_2 - CH_2 - NH - C$$

RN 471244-05-0 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-5-carboxamide, N-[4-[[[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropyl]thio]acetyl]amino]phenyl]-3',6'-dihydroxy-3-oxo-(9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 471244-06-1 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-6-carboxamide, N-[1-[[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3oxopropyl]thio]acetyl]amino]-1-methylethyl]-3',6'-dihydroxy-3-oxo-(9CI) (CA INDEX NAME)

RN 471244-07-2 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-6-carboxylic acid, 3',6'-dihydroxy-3-oxo-, 2-[[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropyl]thio]acetyl]hydrazide (9CI) (CA INDEX NAME)

RN 471244-08-3 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-6-carboxamide, N-[13-[(2,5-dioxo-1-pyrrolidinyl)oxy]-8,13-dioxo-2,5-dioxa-10-thia-7-azatridec-1-yl]-3',6'-dihydroxy-3-oxo-(9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 471244-09-4 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-6-carboxamide,
N-[18-[(2,5-dioxo-1-pyrrolidinyl)oxy]-13,18-dioxo-3,6,9-trioxa-15thia-12-azaoctadec-1-yl]-3',6'-dihydroxy-3-oxo- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

```
IC
     ICM C12Q001-68
     435006000
NCL
     9-1 (Biochemical Methods)
CC
     Section cross-reference(s): 3, 6
     SNP detection primer mass modifier cleavage mass
ST
     spectrometry; multiplex protein analysis probe
     cleavage photosensitizer mass spectrometry
ΙT
     Proteins
        (A, conjugates with probe, as reporter; methods for detecting a
        plurality of analytes by mass spectrometry)
ΙT
     Dyes
        (amine, tagged to the probe; methods for detecting a plurality of
        analytes by mass spectrometry)
ΙT
     Antibodies
        (anti-ligand, conjugated with probe as reporter; methods for
        detecting a plurality of analytes by mass
        spectrometry)
ΙT
     Cytokines
     Interleukin 10
     Interleukin 4
     Interleukin 6
     Interleukin 8
     Tumor necrosis factors
        (antigen anal.; methods for detecting a plurality of analytes by
        mass spectrometry)
ΙT
     Antibodies
     Antigens
     Avidins
     Ligands
     Receptors
        (as reporter, tagged to the probe; methods for detecting a
        plurality of analytes by mass spectrometry)
ΙT
     Photoimaging materials
        (as reporter; methods for detecting a plurality of analytes by
        mass spectrometry)
IT
     Nucleic acids
        (boronate-linked, mass-modified; methods for detecting a
        plurality of analytes by mass spectrometry)
ΙT
     Chemistry
        (chem. compds., chemi-activated sensitizer, as reporter; methods
        for detecting a plurality of analytes by mass
        spectrometry)
ΙΤ
     Metalloporphyrins
        (cleavable sensitizer tagged to the probe; methods for detecting
        a plurality of analytes by mass spectrometry)
IT
     Polynucleotides
        (conjugates with probe, as reporter; methods for detecting a
        plurality of analytes by mass spectrometry)
```

ΙT Bond (covalent, nuclease-resistant, formed between probe and reporter; methods for detecting a plurality of analytes by mass spectrometry) ΙΤ Aldehydes, analysis (deriv., as cleavable reporter conjugated to probe; methods for detecting a plurality of analytes by mass spectrometry) ΙT Light (for reporter cleavage from the probe; methods for detecting a plurality of analytes by mass spectrometry) Amides, analysis ΙT (linkage between reporter and the probe; methods for detecting a plurality of analytes by mass spectrometry) ΙT DNA microarray technology Ion trap mass spectrometry Mass spectrometry Nucleic acid hybridization Quadrupole mass spectrometry Tandem mass spectrometry Time-of-flight mass spectrometry (methods for detecting a plurality of analytes by mass spectrometry) ΙT Carbohydrates, analysis Lipids, analysis Nucleic acids Peptides, analysis Polysaccharides, analysis Proteins (methods for detecting a plurality of analytes by mass spectrometry) ΙΤ Functional groups (phosphodiester, linkage between reporter and the probe; methods for detecting a plurality of analytes by mass spectrometry) ΙT Nucleic acids (phosphoramidate-linked, mass-modified; methods for detecting a plurality of analytes by mass spectrometry) Sulfonic acids, preparation IT(released from reporter cleavage from the probe; methods for detecting a plurality of analytes by mass spectrometry) ΙT Genetic polymorphism (single nucleotide, detection of; methods for detecting a plurality of analytes by mass spectrometry) ΙT Molecules (small, anal. of; methods for detecting a plurality of analytes by mass spectrometry)

ΙT Probes (nucleic acid) (tagged with mass modifier; methods for detecting a plurality of analytes by mass spectrometry) ΙT Nucleic acids (thiophosphate-linked, mass-modified; methods for detecting a plurality of analytes by mass spectrometry) ΙT Interferons (.gamma., antigen anal.; methods for detecting a plurality of analytes by mass spectrometry) ΙΤ 6066-82-6, N-Hydroxysuccinimide (as cleavable reporter conjugated to probe; methods for detecting a plurality of analytes by mass spectrometry) 412319-46-1P ΙT 151890-73-2P 471244-10-7P 471244-11-8P 471244-12-9P 471244-13-0P 471244-14-1P 471244-15-2P 471244-16-3P 471244-17-4P 471244-18-5P 471244-19-6P 471244-2 471244-21-0P 471244-22-1P 471244-23-2P 471244-24-3P 471244-25-4P 471244-26-5P 471244-27-6P (as cleavable reporter conjugated to probe; methods for detecting a plurality of analytes by mass spectrometry) ΙΤ 471244-00-5P 471244-01-6P 471244-02-7P 471244-03-8P 471244-04-9P 471244-05-0P 471244-06-1P 471244-07-2P 471244-08-3P 471244-09-4P (as cleavable reporter conjugated to probe; methods for detecting a plurality of analytes by mass spectrometry) ΙΤ 9013-20-1, Streptavidin (as reporter, tagged to the probe; methods for detecting a plurality of analytes by mass spectrometry) TT 58-85-5D, Biotin, conjugates with oligopeptides (as reporter; methods for detecting a plurality of analytes by mass spectrometry) ΙT 61-73-4, Methylene blue (cleavable sensitizer tagged to the probe; methods for detecting a plurality of analytes by mass spectrometry) ΙT 37228-74-3, Exonuclease (for reporter cleavage from the probe; methods for detecting a plurality of analytes by mass spectrometry) IΤ 9026-81-7, Nuclease (for tag cleavage from the probe; methods for detecting a plurality of analytes by mass spectrometry) ΙT 6303-21-5, Phosphinic acid (linkage between reporter and the probe; methods for detecting a plurality of analytes by mass spectrometry) ΙΤ 119-61-9D, Benzophenone, conjugates with nucleic acid probes 492-22-8D, 9-Thioxanthone, conjugates with nucleic acid probes 523-27-3D, 9,10-Dibromoanthracene, conjugates with nucleic acid

9003-99-0D, Myeloperoxidase, conjugates with nucleic acid

9055-20-3D, Chloroperoxidase, conjugates with nucleic acid

probes

probes

- probes 17372-87-1D, Eosin, conjugates with nucleic acid probes (methods for detecting a plurality of analytes by mass spectrometry)
- 1T 107-96-0, 3-Mercaptopropionic acid 3301-79-9, 6-Carboxyfluorescein 39028-27-8 76823-03-5, 5-Carboxyfluorescein (methods for detecting a plurality of analytes by mass spectrometry)
- ANSWER 8 OF 28 HCA COPYRIGHT 2004 ACS on STN

 137:43912 Acid-labile isotope-coded extractant (ALICE) and its use in quantitative mass spectrometric analysis of protein mixtures. Qiu, Yongchang;
 Wang, Jack H.; Hewick, Rodney M. (Genetics Institute, Inc., USA).
 PCT Int. Appl. Wo 2002048717 A2 20020620, 44 pp. DESIGNATED STATES:
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.
 APPLICATION: WO 2001-US50745 20011022. PRIORITY: US 2000-PV242643
- 20001023. The invention concerns a method which provides novel compds., termed AB acid-labile isotope-coded extractants (ALICE), for quant. mass spectrometric anal. of protein mixts. The compds. contain a thiol-reactive group that is used to capture cysteine-contg. peptides from all peptide mixts., an acid-labile linker, and a non-biol. polymer. One of the two acid-labile linkers is isotopically labeled and therefore enables the direct quantitation of peptides/proteins through mass spectrometric anal. Because no functional proteins are required to capture peptides, a higher percentage of org. solvent can be used to solubilize the **peptides**, particularly hydrophobic peptides, through the binding, washing and eluting steps, thus permitting much better recovery of peptides. Moreover, since the peptides are covalently linked to the non-biol. polymer (ALICE), more stringent washing is allowed in order to completely remove non-specifically bound species. Finally, peptides captured by ALICE are readily eluted from the polymer support under mild acid condition with high yield and permit

the direct down stream mass spectrometric anal.
without any further sample manipulation. In combination with our novel dual column two dimensional liq. chromatog.- mass spectrometry (2D-LC-MS/MS) design, the
ALICE procedure proves to a general approach for quant. mass spectrometric anal. of protein mixts.
with better dynamic range and sensitivity.
436144-21-7D, reaction with polymers 436144-22-8D, reaction with polymers
 (acid-labile isotope-coded extractant (ALICE) and use in quant. mass spectrometric anal.
 of protein mixts.)
436144-21-7 HCA

1H-Pyrrole-1-hexanamide, 2,5-dihydro-N-(3-hydroxy-9H-xanthen-9-yl)-

2,5-dioxo- (9CI) (CA INDEX NAME)

ΙT

RN

CN

RN 436144-22-8 HCA
CN 1H-Pyrrole-1-hexanamide-.alpha.,.alpha.,.beta.,.beta.,.gamma.,.gamma
.,.delta.,.delta.,.epsilon.,.epsilon.-d10, 2,5-dihydro-N-(3-hydroxy-9H-xanthen-9-yl)-2,5-dioxo- (9CI) (CA INDEX NAME)

mass spectrometry

Polymers, analysis

ΙΤ

```
(ALICE (acid-labile isotope-coded extractant);
   acid-labile isotope-coded extractant (ALICE) and use in
   quant. mass spectrometric anal. of
   protein mixts.)
Mass spectrometry
   (HPLC combined with; acid-labile isotope-coded
   extractant (ALICE) and use in quant. mass
   spectrometric anal. of protein
   mixts.)
Digestion, chemical
  Disulfide group
High throughput screening
  Mass spectrometry
Process automation
  Protein degradation
Reduction
Sulfhydryl group
Tandem mass spectrometry
Test kits
Washing
   (acid-labile isotope-coded extractant (ALICE) and use
   in quant. mass spectrometric anal.
   of protein mixts.)
Proteins
   (acid-labile isotope-coded extractant (ALICE) and use
   in quant. mass spectrometric anal.
   of protein mixts.)
Reagents
   (acid-labile isotope-coded extractant (ALICE) and use
   in quant. mass spectrometric anal.
   of protein mixts.)
Enzymes, uses
   (acid-labile isotope-coded extractant (ALICE) and use
   in quant. mass spectrometric anal.
   of protein mixts.)
Isotopes
  Polyoxyalkylenes, properties
   (acid-labile isotope-coded extractant (ALICE) and use
   in quant. mass spectrometric anal.
   of protein mixts.)
Peptides, analysis
   (cysteine-contg.; acid-labile isotope-coded
   extractant (ALICE) and use in quant. mass
   spectrometric anal. of protein
   mixts.)
Mass spectrometry
   (liq. chromatog. combined with; acid-labile isotope
   -coded extractant (ALICE) and use in quant. mass
```

ΙT

ΤТ

ΙT

ΙΤ

IT

ΙΤ

ΙΤ

ΙT

```
spectrometric anal. of protein
        mixts.)
ΙΤ
     HPLC
     Liquid chromatography
         (mass spectrometry combined with; acid-labile
        isotope-coded extractant (ALICE) and use in quant.
        mass spectrometric anal. of
        protein mixts.)
ΙT
     Albumins, analysis
        (serum; acid-labile isotope-coded extractant (ALICE)
        and use in quant. mass spectrometric
        anal. of protein mixts.)
ΙT
     Halogen compounds
        (.alpha.-halo-acetyl; acid-labile isotope-coded
        extractant (ALICE) and use in quant. mass
        spectrometric anal. of protein
        mixts.)
ΙT
     436144-21-7D, reaction with polymers 436144-22-8D,
     reaction with polymers
        (acid-labile isotope-coded extractant (ALICE) and use
        in quant. mass spectrometric anal.
        of protein mixts.)
ΙT
               9002-07-7, Trypsin
     2949-92-0
        (acid-labile isotope-coded extractant (ALICE) and use
        in quant. mass spectrometric anal.
        of protein mixts.)
ΙΤ
     541-59-3, Maleimide 7782-39-0, Deuterium,
     properties 9003-53-6, Polystyrene 25322-68-3,
     Polyethylene glycol
        (acid-labile isotope-coded extractant (ALICE) and use
        in quant. mass spectrometric anal.
        of protein mixts.)
     438064-53-0
IT
        (unclaimed protein sequence; acid-labile
        isotope-coded extractant (ALICE) and its use in quant.
        mass spectrometric anal. of
        protein mixts.)
ΙT
     81183-26-8
                 435314-09-3 435314-15-1 435314-17-3
                                                            437984-21-9
     437984-22-0
                  437984-23-1 437984-24-2
                                              437984-25-3
                                                            437984-26-4
     437984-27-5
                 437984-28-6 437984-29-7 437984-30-0
                                                             437984-31-1
        (unclaimed sequence; acid-labile isotope-coded
        extractant (ALICE) and its use in quant. mass
        spectrometric anal. of protein
       mixts.)
L98
    ANSWER 9 OF 28 HCA COPYRIGHT 2004 ACS on STN
          Isotope-coded ionization-enhancing reagents (ICIER)
137:17454
```

for high-throughput protein identification and

```
Wallenhorst 10/045,170
                                                          date god
quantitation using matrix-assisted laser desorption
ionization mass spectrometry. Qiu, Yongchang;
Wang, Jack H.; Hewick, Rodney M. (Genetics Institute, LLC, USA).
PCT Int. Appl. WO 2002046770 A2 20020613, 45 pp. DESIGNATED STATES:
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
W. AE, AG, AH, AH, AH, AG, AG, EC, EE, ES, FI, GB, GD, GE, GH, GM, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM,
HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG,
 CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML,
 MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.
 APPLICATION: WO 2001-US50744 20011022. PRIORITY: US 2000-PV242645
  The invention concerns arginine-contg. cysteine-modifying
  compds. useful for MALDI-MS anal. of
  proteins are provided. These compds. termed isotope
  -coded ionization enhancement reagents (ICIER) can provide
  ionization enhancement in MALDI-MS, relative quantitation,
  and addnl. database searching constraints at the same time without
  any extra sample manipulation. More specifically, ICIER increase
   the ionization efficiency of cysteine-contg.
   peptides by attachment of a guanidino functional group.
   ICIER also increase the overall hydrophilicity of these
   peptides due the hydrophilic nature of ICIER and thus
   increase the percentage of recovery of these peptides
   during sample handling and processing such as in-gel
   digestion or liq. chromatog. Finally, a combination of both
    light and heavy ICIER provides an accurate way to obtain relative
    quantitation of proteins by MALDI-MIS and addnl.
    database searching constraints (no. of cysteine residues
    in every single peptide peak) to increase the confidence
    of protein identification by peptide
        (isotope-coded ionization-enhancing reagents (ICIER)
    mass mapping.
     7782-39-0, Deuterium, uses
        for high-throughput protein identification
TI
        and quantitation using matrix-assisted laser desorption
        ionization mass spectrometry)
     Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME)
     7782-39-0 HCA
RN
CN
 D- D
          (isotope-coded ionization-enhancing reagents (ICIER)
      52-90-4, Cysteine, properties
          for high-throughput protein identification
 TT
```

and quantitation using matrix-assisted laser desorption ionization mass spectrometry)

RN 52-90-4 HCA

4 3

CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IC ICM G01N033-68

CC 9-16 (Biochemical Methods)
Section cross-reference(s): 6

ST ionization reagent high throughput screening protein MALDI mass spectrometry

IT Gel electrophoresis

(PAGE; isotope-coded ionization-enhancing reagents (ICIER) for high-throughput protein identification and quantitation using

matrix-assisted laser desorption ionization mass

spectrometry)

IT Peptides, analysis

(cysteine-contg.; isotope-coded

ionization-enhancing reagents (ICIER) for high-throughput

protein identification and quantitation

using matrix-assisted laser desorption ionization mass spectrometry)

IT Functional groups

(guanidino group; isotope-coded ionization-enhancing

reagents (ICIER) for high-throughput protein

identification and quantitation using

matrix-assisted laser desorption ionization mass

spectrometry)

IT Amide group

Amino group

Carboxyl group

Chemical chains

Digestion, chemical

Disulfide group

High throughput screening

Ionization

Labels

Mass spectrometry

Molecular association

Radiochemical analysis

Sample preparation Sulfhydryl group Test kits (isotope-coded ionization-enhancing reagents (ICIER) for high-throughput protein identification and quantitation using matrix-assisted laser desorption ionization mass spectrometry) Peptides, analysis Proteins (isotope-coded ionization-enhancing reagents (ICIER) for high-throughput protein identification and quantitation using matrix-assisted laser desorption ionization mass spectrometry) Isotopes (isotope-coded ionization-enhancing reagents (ICIER) for high-throughput protein identification and quantitation using matrix-assisted laser desorption ionization mass spectrometry) Reagents (isotope-coded ionization-enhancing reagents (ICIER) for high-throughput protein identification and quantitation using matrix-assisted laser desorption ionization mass spectrometry) Functional groups (maleimide; isotope-coded ionization-enhancing reagents (ICIER) for high-throughput protein identification and quantitation using matrix-assisted laser desorption ionization mass spectrometry) Laser ionization mass spectrometry (photodesorption, matrix-assisted; isotope-coded ionization-enhancing reagents (ICIER) for high-throughput protein identification and quantitation using matrix-assisted laser desorption ionization mass spectrometry) Laser desorption mass spectrometry (photoionization, matrix-assisted; isotope-coded ionization-enhancing reagents (ICIER) for high-throughput protein identification and quantitation using matrix-assisted laser desorption ionization mass spectrometry) Functional groups (.alpha.-haloacetyl; isotope-coded ionization-enhancing reagents (ICIER) for high-throughput protein identification and quantitation using matrix-assisted laser desorption ionization mass spectrometry) 7782-39-0, Deuterium, uses

ΙT

ΙT

ΙT

IT

ΙT

ΙΤ

ΙT

ΙΤ

```
(isotope-coded ionization-enhancing reagents (ICIER)
         for high-throughput protein identification
         and quantitation using matrix-assisted laser desorption
         ionization mass spectrometry)
ΙT
      434335-16-7P
                    434335-17-8P
                                    434335-18-9P
     434335-20-3P
                                                   434335-19-0P
        (isotope-coded ionization-enhancing reagents (ICIER)
        for high-throughput protein identification
        and quantitation using matrix-assisted laser desorption
        ionization mass spectrometry)
ΙT
     9001-92-7, Proteinase
        (isotope-coded ionization-enhancing reagents (ICIER)
        for high-throughput protein identification
       and quantitation using matrix-assisted laser desorption
       ionization mass spectrometry)
ΙT
    52-90-4, Cysteine, properties
       (isotope-coded ionization-enhancing reagents (ICIER)
       for high-throughput protein identification
       and quantitation using matrix-assisted laser desorption
       ionization mass spectrometry)
Τ ]
    161181-39-1
                  435313-81-8
                                435313-83-0
    435313-89-6
                 435313-91-0
                                              435313-85-2
                                                            435313-87-4
                                435313-93-2
    435313-99-8 435314-01-5
                                              435313-95-4
                                                            435313-97-6
                                435314-03-7
    435314-09-3
                                              435314-05-9
                  435314-12-8
                                                            435314-07-1
                                435314-14-0
    435314-17-3
                                              435314-15-1
                 435314-18-4
                                                            435314-16-2
                                435314-19-5
       (unclaimed sequence; isotope-coded ionization-enhancing
                                                            435314-27-5
      reagents (ICIER) for high-throughput protein
      identification and quantitation using
      matrix-assisted laser desorption ionization mass
86
  ANSWER 10 OF 28 HCA COPYRIGHT 2004 ACS on STN
66:366139 Labeled peptides, proteins and antibodies and processes and
   intermediates useful for their preparation. Hahn, Klaus M.;
  Toutchkine, Alexei; Muthyala, Rajeev; Kraynov, Vadim; Bark, Steven
  J.; Burton, Dennis R.; Chamberlain, Chester (USA). U.S. Pat. Appl.
  Publ. US 2002055133 Al 20020509, 54 pp., Cont.-in-part of Appl. No.
  PCT/US2000/26821. (English). CODEN: USXXCO. APPLICATION: US
                         PRIORITY: US 2000-PV218113 20000713; WO
  2000-US26821 20000929.
  The invention provides peptide synthons having protected functional
  groups for attachment of desired moieties (e.g. functional mols. or
  probes). Also provided are peptide conjugates prepd. from such
  synthons, and synthon and conjugate prepn. methods including
 procedures for identifying the optimum probe attachment site.
 Biosensors are provided having environmentally sensitive dyes that
 can locate specific biomols. within living cells and detect chem.
 and physiol. changes in those biomols. as the living cell is moving,
```

metabolizing and reacting to its environment. Methods are included for detecting GTP activation of a Rho GTPase protein using polypeptide biosensors. When the biosensor binds GTP-activated Rho GTPase protein, the environmentally sensitive dye emits a signal of a different lifetime, intensity or wavelength than when not bound. New fluorophores whose fluorescence responds to environmental changes are also provided that have improved detection and attachment properties, and that can be used in living cells, or in vitro.

IT 4091-99-ODP, DCFH, conjugates

(DCFH; labeled peptides and proteins and antibodies and processes and intermediates useful in their prepn.)

- RN 4091-99-0 HCA
- CN Benzoic acid, 2-[3,6-bis(acetyloxy)-2,7-dichloro-9H-xanthen-9-yl]- (9CI) (CA INDEX NAME)

- IC G01N033-53; G01N033-537; G01N033-543; C07D417-02; C07K014-435
- NCL 435079200
- CC 9-14 (Biochemical Methods)

Section cross-reference(s): 1, 7, 34, 41

IT Imagino

(FLAIR (fluorescent activation indicator for Rho proteins); labeled peptides and proteins and antibodies and processes and intermediates useful in their prepn.)

IT 4091-99-0DP, DCFH, conjugates

(DCFH; labeled peptides and proteins and antibodies and processes and intermediates useful in their prepn.)

IT 423205-43-0P

(amino acid sequence, cloning and site-specific **cysteine** mutagenesis of; labeled peptides and proteins and antibodies and processes and intermediates useful in their prepn.)

- L98 ANSWER 11 OF 28 HCA COPYRIGHT 2004 ACS on STN
- 136:196571 Highly homogeneous molecular markers for electrophoresis. Tadayoni-Rebek, Mitra; Amshey, Joseph W.; Rooney, Regina (Invitrogen Corporation, USA). PCT Int. Appl. WO 2002013848 Al 20020221, 64 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR,

BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English).

CODEN: PIXXD2. APPLICATION: WO 2001-US25276 20010813. PRIORITY: US 2000-PV224345 20000811.

AB The invention relates to marker mols. for identifying phys. properties of mol. species sepd. by the use of electrophoretic systems. The invention further relates to methods for prepg. and using marker mols. Peptide Cys-Leu-Lys(TMR)-Asp-Ala-Leu-Asp-Ala-Leu-Asp-Ala-Leu-Asp-Ala-Leu-Lys(TMR)-Asp-Ala was prepd. by solid phase peptide synthesis and ligated with a recombinant 95-amino acid maltose-binding protein to make a marker protein with pI 4.75.

IT 401466-24-8

(highly homogeneous mol. markers for electrophoresis)

RN 401466-24-8 HCA

CN Xanthylium, 9-[2-carboxy-4(or 5)-[[[(5S)-6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-5-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-6-oxohexyl]amino]carbonyl]phenyl]-3,6-bis(dimethylamino)-, inner salt (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

ΙΤ 52-90-4, Cysteine, properties

(labeling mol. contg. N-terminal; highly homogeneous mol. markers for electrophoresis)

52-90-4 HCA RN

L-Cysteine (9CI) (CA INDEX NAME) CN

Absolute stereochemistry.

- IC ICM A61K038-16
- 9-7 (Biochemical Methods) CC

Section cross-reference(s): 34

- ST homogeneous mol marker electrophoresis; protein marker electrophoresis isoelec point; maltose binding protein ligation labeled peptide
- Proteins ΙT

(MBP (maltose-binding protein), 95-amino acid, ligation with TMR-labeled peptide; highly homogeneous mol. markers for electrophoresis) Linking agents ΙT (between label component and protein or nucleic acid; highly homogeneous mol. markers for electrophoresis) ΙT (for 95-amino acid maltose binding protein; highly homogeneous mol. markers for electrophoresis) IT(highly homogeneous mol. markers for electrophoresis) ΙΤ Amino acids, preparation Nucleic acids Peptides, preparation Proteins (labeled; highly homogeneous mol. markers for electrophoresis) Peptides, preparation IT(oligopeptides, labeled, prepn. and ligation to protein ; highly homogeneous mol. markers for electrophoresis) ΙΤ Test kits (protein marker kits; highly homogeneous mol. markers for electrophoresis) ΙT 401466-17-9 401466-24-8 (highly homogeneous mol. markers for electrophoresis) 52-90-4, Cysteine, properties ΙΤ (labeling mol. contg. N-terminal; highly homogeneous mol. markers for electrophoresis) 401466-22-6P ΙT (ligation with 95-amino acid maltose-binding protein to make marker protein; highly homogeneous mol. markers for electrophoresis) 401466-07-7P 401466-09-9P 401466-12-4P 401466-03**-**3P IT 401466-14-6P (prepn. and ligation with maltose-binding protein to make marker protein; highly homogeneous mol. markers for electrophoresis) ANSWER 12 OF 28 HCA COPYRIGHT 2004 ACS on STN L98 136:163716 Labeled peptides, proteins and antibodies and processes and intermediates useful for their preparation. Klaus M.; Toutchkine, Alexei; Muthyala, Rajeev; Kraynov, Vadim; Bark, Steven J.; Burton, Dennis R.; Chamberlain, Chester (The Scripps Research Institute, USA). PCT Int. Appl. WO 2002008245 A2 20020131, 158 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU,

AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,

TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, (English). CODEN: PIXXD2. APPLICATION: WO 2001-US22194 TG, TR. PRIORITY: US 2000-PV218113 20000713; WO 2000-US26821 20010713. 20000929; US 2001-PV279302 20010328; US 2001-839577 20010420. The invention provides peptide synthons having protected functional AB groups for attachment of desired moieties (e.g. functional mols. or probes). Also provided are peptide conjugates prepd. from such synthons, and synthon and conjugate prepn. methods including procedures for identifying optimum probe attachment sites. Biosensors are provided having functional mols. that can locate and bind to specific biomols. within living cells. Biosensors can detect chem. and physiol. changes in those biomols. as living cells are moving, metabolizing and reacting to its environment. are included for detecting GTP activation of a Rho GTPase protein using polypeptide biosensors. When the biosensor binds GTP-activated Rho GTPase protein, an environmentally sensitive dye emits a signal of a different lifetime, intensity or wavelength than when not bound. New fluorophores whose fluorescence responds to environmental changes are also provided that have improved detection and attachment properties, and that can be used in living cells, or in vitro. ΙΤ

393512-12-4

(labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.)

393512-12-4 HCA RN

Benzoic acid, 2,3,5-trichloro-4-[[2-[[6-[(2,5-dihydro-2,5-dioxo-1H-CNpyrrol-1-yl)oxy]-6-oxohexyl]amino]-2-oxoethyl]thio]-6-[1,3,4,8,9,10hexahydro-2,2,4,8,10,10-hexamethyl-12,14-disulfo-2H-pyrano[3,2-q:5,6q']diquinolin-6-yl]-, monosodium salt (9CI) (CA INDEX NAME)

Na

IC ICM C07K001-00

9-14 (Biochemical Methods) CC Section cross-reference(s): 7, 15, 34, 41

labeled peptide protein antibody prepn; biosensor ST targeting biomol living cell probe; GTP activation Rho GTPase detection polypeptide biosensor; fluorophore fluorescence probe environmental change living cell

ΙT Animal cell line

> (3T3; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.)

Fluorescent dyes ΙΤ

(Alexa, conjugates with polypeptides; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.)

ΙΤ Imaging

> (FLAIR (fluorescent activation indicator for Rho proteins); labeled peptides, proteins and

antibodies and processes and intermediates useful for prepn.)

Transcription factors IT

> (GCN4, peptide tag derived from leucine zipper of; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.)

ΙT Histocompatibility antigens

> (HLA-B27, fusion proteins with GFP; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.)

ΙT Immunoglobulin receptors

(IgE type I; labeled peptides, proteins and antibodies

and processes and intermediates useful for prepn.) ΙT Resins (MBHA; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) Histocompatibility antigens ΙT (MHC (major histocompatibility complex); labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Phycoerythrins (P; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙΤ Phycoerythrins (R-phycoerythrins, conjugates with peptides; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Imaging (Rac activation in cells; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙΤ Wound healing (Rac role in; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) G proteins (guanine nucleotide-binding proteins) ΤТ (Rac, polypeptide biosensor as p21-activated kinase peptide binding to; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Proteins (WASP (Wiskott-Aldrich syndrome protein), polypeptide biosensor as peptide of, binding to cdc42; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙΤ Functional groups (aminooxy, peptide contq.; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Neutrophil (assay of cdc42 activity in cell lysates of stimulated; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Physics (biophysics, probes; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙΤ Proteins (cellular, localization in living cells; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Allophycocyanins Phycoerythrins (conjugates with peptides; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.)

ΙT Drugs (conjugates with polypeptides; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Antibodies Peptides, biological studies Polynucleotides Proteins (conjugates; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT (cyan fluorescent protein, conjugates, polypeptide biosensor contq.; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) TΤ Fluorescent dyes (cyanine, conjugates with peptides; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Gene (encoding fusion proteins; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Proteins (enhanced green fluorescent protein, conjugates, polypeptide biosensor contg.; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Proteins (enhanced yellow green fluorescent protein, conjugates, polypeptide biosensor contg.; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Cyanine dyes (fluorescent, conjugates with peptides; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙΤ Fluorescent substances (fluorophores, for detecting changes in responses of living cells to environment; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Immunoglobulins (fragments, conjugates; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙΤ Rho protein (G protein) (fusion proteins with fluorescent proteins; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) G proteins (guanine nucleotide-binding proteins) . IT (gene CDC42; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Rho protein (G protein)

(gene RhoA; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Proteins (green fluorescent, conjugates, polypeptide biosensor contg.; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Nucleic acids (indicators for, conjugates with polypeptides; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Biosensors Blood serum Cell Cell migration Endoplasmic reticulum Fibroblast Fluorescence Fluorescence excitation Fluorescence resonance energy transfer Fluorescent dyes Genetic vectors Human Phosphorescence Phosphorescent substances Signal transduction, biological Stress, animal Stress, microbial Stress, plant (labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Actins Calmodulins Mvosins (labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Peptides, biological studies (labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙΤ DNA Proteins RNA (labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) IΤ Antibodies Antigens (labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Platelet-derived growth factors

(labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Nucleic acids (labeled; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) IT Antibodies (labeled; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) Peptides, biological studies ΙT (labeled; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Proteins (labeled; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ITProtein motifs (leucine zipper, polypeptide biosensor contg.; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Fusion proteins (chimeric proteins) (of Rho GTPase protein and fluorescent proteins ; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) IT Affinity (of peptide conjugate for target; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Actins (polymn., Rac1 activation localization at site of; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Ligands (polypeptide-dye conjugates sensitive to binding by; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) IT (polypeptide-dye conjugates sensitive to; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT ESR (electron spin resonance) (probes, conjugates with polypeptides; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) IT Protein motifs (protein-binding domain of p21-activated kinase 1, polypeptide biosensor contq.; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) Phosphorylation, biological IT(protein; labeled peptides, proteins and

antibodies and processes and intermediates useful for prepn.) ΙT Proteins (red fluorescent protein, conjugates, polypeptide biosensor contq.; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Sensors (responsive, conjugates with polypeptides; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Dyes (sensitive to pH or ligand binding or other, conjugates with polypeptides; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Cage compounds (sensors, conjugates with polypeptides; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Dyes (solvatochromic, conjugates with polypeptides; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT Proteins (yellow green fluorescent protein, conjugates, polypeptide biosensor contg.; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙΤ Actinins (.alpha.-; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙΤ Lactoglobulins (.beta.-, labeling with tetramethylrhodamine N-hydroxysuccinimide ester; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT 144713-51-9, Erk4 protein kinase (Erk4 protein kinase; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT 9059-32-9DP, GTPase, conjugates with fluorescent proteins (GTP-activated Rho; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT 394257-19-3P (amino acid sequence of peptide tag derived from GCN4 leucine zipper; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT 271795-11-0P (amino acid sequence, C-terminal p21 binding domain peptide; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙΤ 393511-94-9P

(amino acid sequence, N-terminal p21 binding domain peptide; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) 394257-16-0 IT(amino acid sequence, as tag in cellular protein localization; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT 394257-20-6P (amino acid sequence, cloning and site-specific cysteine mutagenesis of; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) ΙT 394257-21-7 (amino acid sequence; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) 393512-09-9 393512-10-2 393512-11-3 ΙT 393512-08-8 (as merocyanine dye; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) 76-05-1, Trifluoroacetic acid, uses 5961-85-3, ΙT Tris(2-carboxyethyl)phosphine (in eliminating multiply-labeled side products; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) IT50-01-1P, Guanidine hydrochloride (in improving yield of labeled product; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) 9004-07-3, .alpha.-Chymotrypsin ΙT 9002-07-7, Trypsin (labeled peptide cleavage with; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) 137632-07-6, Erkl kinase 144713-50-8, Erk3 protein ΙT kinase (labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) 137632-08-7, Erk2 kinase ΙT (labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) 394257-19-3DP, tetramethylrhodamine-labeled ΙT (labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) 65-61-2DP, Acridine Orange, conjugates with peptides 1239-45-8DP, IT1325-87-7DP, Cascade Ethidium Bromide, conjugates with peptides 1461-15-ODP, Calcein, conjugates Blue, conjugates with peptides 2321-07-5DP, Fluorescein, conjugates with peptides with peptides 2768-89-0DP, Rhodamine X, conjugates with peptides 3520-42-1DP, Lissamine Rhodamine B, conjugates with peptides 7059-24-7DP,

Chromomycin A3, conjugates with peptides 7240-37-1DP, 7-AAD, conjugates with peptides 10199-91-4DP, NBD, conjugates with

18378-89-7DP, Mithramycin, conjugates with peptides 23491-45-4DP, Hoechst 33258, conjugates with peptides 23491-52-3DP, Hoechst 33342, conjugates with peptides 25535-16-4DP, Propidium Iodide, conjugates with peptides 30230-57-0DP, conjugates with peptides 41085-99-8DP, conjugates 43070-85-5DP, Hydroxycoumarin, conjugates with with peptides peptides 47165-04-8DP, DAPI, conjugates with peptides 51908-46-4DP, Dansyl aziridine, conjugates with peptides 70281-37-7DP, Tetramethylrhodamine, conjugates with peptides 76421-73-3DP, Monochlorobimane, conjugates with peptides 76433-29-9DP, LDS 751, conjugates with peptides 82354-19-6DP, Texas Red, conjugates with peptides 82446-52-4DP, Lucifer Yellow, 96314-96-4DP, Indo-1, conjugates with conjugates with peptides 96314-98-6DP, Fura-2, conjugates with peptides 107091-89-4DP, Thiazole Orange, conjugates with peptides 107347-53-5DP, TRITC, conjugates with peptides 112117-57-4DP, 123632-39-3DP, Fluo-3, conjugates with conjugates with peptides 126208-12-6DP, Carboxy-SNARF-1, conjugates with peptides peptides 143245-02-7DP, conjugates with peptides 143413-84-7DP, TOTO-1, conjugates with peptides 143413-85-8DP, YOYO-1, conjugates with 146368-15-2DP, Cy5, conjugates with peptides peptides 146368-16-3DP, Cv3, conjugates with peptides 149838-22-2DP, FM 1-43, conjugates with peptides 153967-04-5DP, SNARF, conjugates 157199-59-2DP, TO-PRO-1, conjugates with peptides with peptides 157199-63-8DP, TO-PRO-3, conjugates with peptides 165599-63-3DP, BODIPY-FL, conjugates with peptides 166196-17-4DP, TOTO-3, conjugates with peptides 169799-14-8DP, Cy7, conjugates with 194100-76-0DP, SYTOX Green, conjugates with peptides peptides 204934-16-7DP, BODIPY TR, conjugates with peptides 237752-36-2DP, Red 613, conjugates with peptides 247145-11-5DP, Alexa-532, 287384-28-5DP, BODIPY TMR, conjugates conjugates with peptides 324767-53-5DP, SYTOX Orange, conjugates with with peptides 396076-95-2DP, TruRed, conjugates with peptides peptides 396077-00-2DP, SYTOX Blue, conjugates with peptides (labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) 393511-95-0P (labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) 56-65-5, ATP, biological studies 86-01-1, GTP 22537-22-0, Magnesium ion, biological studies 142805-58-1, MEK kinase (labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) 393511-96-1DP, ditetramethylrhodamine-labeled 393511-97-2P (labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.) 64-19-7, Acetic acid, uses 7440-66-6, Zinc, uses (labeled peptides, proteins and antibodies and

ΙΤ

ΙT

ΙT

ΙT

```
processes and intermediates useful for prepn.)
ΙT
                    271795-10-9P
                                   393511-92-7P
     271795-07-4P
                                                  393511-93-8P
     393511-96-1P
                    394257-17-1P
                                   394656-50-9P
                                                  394656-72-5P
        (labeled peptides, proteins and antibodies and
        processes and intermediates useful for prepn.)
IT
     393511-93-8DP, tetramethylrhodamine-labeled
                                                   394656-50-9DP,
     tetramethylrhodamine-labeled
                                    394679-45-9P
        (labeled peptides, proteins and antibodies and
        processes and intermediates useful for prepn.)
ΙT
     1080-74-6, 3-(Dicyanomethylene)indan-1-one
                                                 1127-35-1
     N-Methylhydroxylamine hydrochloride
                                           5292-43-3 13139-15-6
     17576-35-1, 1,3,3-Trimethoxy propene 27144-18-9
                                                         73259-81-1
     246256-50-8
                 271795-14-3
                                393512-00-0
                                               393512-07-7
     393512-12-4
        (labeled peptides, proteins and antibodies and
        processes and intermediates useful for prepn.)
                    271795-04-1P
                                  271795-05-2P
ΙT
     271795-03-0P
                                                  393511-98-3DP,
                   393511-99-4DP, resin-bound 393512-01-1P
     resin-bound
     393512-04-4P
                    394257-18-2P
        (labeled peptides, proteins and antibodies and
        processes and intermediates useful for prepn.)
                    393512-03-3P
                                   393512-05-5P
ΙT
     393512-02-2P
                                                  393512-06-6P
        (labeled peptides, proteins and antibodies and
        processes and intermediates useful for prepn.)
ΙΤ
     9059-32-9, GTPase
        (of Rho protein; labeled peptides, proteins
        and antibodies and processes and intermediates useful for prepn.)
     70-18-8, Glutathione, miscellaneous
ΙT
        (peptide not; labeled peptides, proteins and antibodies
        and processes and intermediates useful for prepn.)
ΙT
     177893-51-5P, p21-Activated kinase
        (polypeptide biosensor as peptide of, binding to Rac; labeled
        peptides, proteins and antibodies and processes and
        intermediates useful for prepn.)
ΙT
     142243-02-5, MAP kinase
        (polypeptide biosensor; labeled peptides, proteins and
        antibodies and processes and intermediates useful for prepn.)
ΙT
     394292-00-3
                   394292-01-4
                                 394292-02-5
                                               394292-03-6
                                                             394292-04-7
     394292-05-8
                   394292-06-9
                                 394292-07-0
                                               394292-08-1
        (unclaimed nucleotide sequence; labeled peptides,
       proteins and antibodies and processes and intermediates
        useful for their prepn.)
                   394291-98-6
                                 394291-99-7
ΙT
     394291-97-5
        (unclaimed protein sequence; labeled peptides,
        proteins and antibodies and processes and intermediates
        useful for their prepn.)
ΙT
     394211-44-0
                   394211-45-1
        (unclaimed sequence; labeled peptides, proteins and
```

antibodies and processes and intermediates useful for their prepn.)

- L98 ANSWER 13 OF 28 HCA COPYRIGHT 2004 ACS on STN

 136:147493 Compounds and methods of non-invasive diagnostic imaging.
 Bridon, Dominique P.; Blanchard, Dominique; Ezrin, Alan M.;
 Pouletty, Phillipe (Can.). U.S. Pat. Appl. Publ. US 2002018751 A1
 20020214, 12 pp., Cont.-in-part of U.S. Ser. No. 588,912, abandoned.
 (English). CODEN: USXXCO. APPLICATION: US 1999-327764 19990607.
 PRIORITY: US 1993-137821 19931015; US 1994-237346 19940503; US
 1995-477900 19950607; US 1996-588912 19960112.
- AΒ The invention concerns compns. and methods of non-invasive diagnosis are provided. The imaging agents include a linking groups and a reactive entity capable of reaction with a reactive functionality to form a covalent bond therewith. The imaging agents may be in the form of a bifunctional anchor mol. The bifunctional anchor mols. have a functional group capable of activation which, when activated, may form a covalent bond with a reactive functionality on a target protein present in the mammalian vascular system, thereby "anchoring" the mol. to that target protein. bifunctional anchors are also conjugated, either directly or indirectly, to a diagnostic agent of interest which provides the ability to diagnostically and non-invasively image the mammalian vascular space. Vascular targets include both cellular- and noncellular-assocd. proteins present in the mammalian vascular system. The methods find use for numerous applications arising from the ability to diagnostically image the mammalian vascular space over an extended period of time or to preferentially diagnostically image only a specific cell type or compartment of the mammalian vascular space.
- IT 244760-42-7

(compds. and methods of non-invasive diagnostic imaging)

- RN 244760-42-7 HCA
- CN Xanthylium, 3,6-diamino-9-[2-carboxy-4(or 5)-[[[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]amino]carbonyl]phenyl]-, chloride (9CI) (CA INDEX NAME)

C1 =

IC ICM A61K049-00

NCL 424009100

CC 9-14 (Biochemical Methods)
Section cross-reference(s): 8, 14

ST imaging diagnosis agent radioisotope mammal vascular covalent bond

L98 ANSWER 14 OF 28 HCA COPYRIGHT 2004 ACS on STN

135:223698 Proteomics based on selecting and quantifying cysteine containing peptides by covalent chromatography. Wang, S.; Regnier, F. E. (Department of Chemistry, Purdue University, Lafayette, IN, 47907, USA). Journal of Chromatography, A, 924(1-2), 345-357 (English) 2001. CODEN: JCRAEY. ISSN: 0021-9673. Publisher: Elsevier Science B.V..

This paper describes a procedure in which cysteine contg.

peptides from tryptic digests of complex protein

mixts. were selected by covalent chromatog. based on thiol
disulfide exchange, identified by mass

spectrometry, and quantified by differential isotope

labeling. Following disruption of disulfide bridges with

2,2'-dipyridyl disulfide, all proteins were

digested with trypsin and acylated with succinic anhydride.

Cysteine contg. peptides were then selected from

the acylated digest by disulfide interchange

with sulfhydryl groups on a thiopropyl Sepharose gel. Captured cysteine contg. peptides were released from the gel with 25 mM dithiothreitol (pH 7.5) contq. 1 mM (ethylenedinitrilo) tetraacetic acid disodium salt and alkylated with iodoacetic acid subsequent to fractionation by reversed-phase lig. chromatog. (RPLC). Fractions collected from the RPLC column were analyzed by matrix-assisted laser desorption ionization mass spectrometry. Based on isotope ratios of peptides from exptl. and control samples labeled with succinic and deuterated succinic anhydride, resp., it was possible to det. the relative concn. of each peptide species between the two samples. Peptides obtained from proteins that were up-regulated in the exptl. sample were easily identified by an increase of the relative amt. of the deuterated peptide. The results of these studies indicate that by selecting cysteine contg. peptides, the complexity of protein digest could be reduced and database searches greatly simplified. When coupled with the isotope labeling strategy for quantification it was possible to det. proteins that were up-regulated in plasmid bearing Escherichia coli when expression of plasmid proteins was induced. Up-regulation of several proteins of E. coli origin was also noted. 9-16 (Biochemical Methods)

CC

ST proteome detection covalent chromatog MALDI mass spectrometry

ΙT Chromatography

> (covalent; proteomics based on selecting and quantifying cysteine contq. peptides by covalent chromatoq.)

ΙT Laser ionization mass spectrometry

> (photodesorption, matrix-assisted; proteomics based on selecting and quantifying cysteine contg. peptides by covalent chromatog.)

Laser desorption mass spectrometry IT

> (photoionization, matrix-assisted; proteomics based on selecting and quantifying cysteine contg. peptides by covalent chromatog.)

TΤ Databases

Escherichia coli

Reversed phase liquid chromatography

Sulfhydryl group

(proteomics based on selecting and quantifying cysteine contq. peptides by covalent chromatoq.)

ITProteins, general, analysis

> (proteomics based on selecting and quantifying cysteine contg. peptides by covalent chromatog.)

ΙΤ 484 - 42 - 49001-63-2, Lysozyme 71800-36-7, 1-9-Kallidin 75909-25-0 76310-14-0, 1-6-Adrenorphin (human) 117620-76-5 359706-65-3 359706-67-5

(proteomics based on selecting and quantifying cysteine contg. peptides by covalent chromatog.)

IT 2127-03-9, 2,2'-Dipyridyl disulfide

(proteomics based on selecting and quantifying cysteine contg. peptides by covalent chromatog.)

ANSWER 15 OF 28 HCA L98 COPYRIGHT 2004 ACS on STN 134:362292 Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile. Farr, Spencer (Phase-1 Molecular Toxicology, USA). PCT Int. Appl. WO 2001032928 A2 20010510, 222 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US30474 20001103. PRIORITY: US 1999-PV165398 19991105; US 2000-PV196571 20000411. AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to det. the hypersensitivity of individuals to a given agent, such as drug or other chem., in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes assocd. with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes assocd. with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or The gene expression profile may be obtained by using an array

a subject are also disclosed. IT 298-50-0, Propantheline

(methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

RN 298-50-0 HCA

CN 2-Propanaminium, N-methyl-N-(1-methylethyl)-N-[2-[(9H-xanthen-9-ylcarbonyl)oxy]ethyl]- (9CI) (CA INDEX NAME)

of nucleic acid probes for the plurality of genes assocd. with hypersensitivity. The expression of the genes predetd. to be

repair of toxic damage at the tissue, organ or system level.

assocd. With hypersensitivity is directly related to prevention or

databases arrays and app. useful for identifying hypersensitivity in

IC ICM C12Q001-68

ICS G01N033-50

CC 3-4 (Biochemical Genetics)

Section cross-reference(s): 1, 6, 7, 13, 15

IT Multidrug resistance proteins

(BCRP (breast cancer resistance protein); methods of

detg. individual hypersensitivity to a pharmaceutical
agent from gene expression profile)

IT Glycoproteins, specific or class

(C4bp (complement C4b-binding protein); methods of

detg. individual hypersensitivity to a pharmaceutical
agent from gene expression profile)

IT Proteins, specific or class

(CAP (adenylate cyclase-assocd. protein); methods of

detg. individual hypersensitivity to a pharmaceutical

agent from gene expression profile)

IT Gene, animal

(G/T mismatch binding protein; methods of detg

. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

IT Cyclins

(G1, cyclin G1 interacting protein; methods of

detg. individual hypersensitivity to a pharmaceutical

agent from gene expression profile)

IT Proteins, specific or class

(GT mismatch binding protein; methods of detg

. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

IT Proteins, specific or class

(L-FABP (liver fatty acid-binding protein); methods of

detg. individual hypersensitivity to a pharmaceutical
agent from gene expression profile)

IT Cytokines

(MBP (major basic protein); methods of detg.

individual hypersensitivity to a pharmaceutical agent from gene

expression profile)

IT Proteins, specific or class

(Nucleosome assembly protein; methods of detg

. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

IT Proteins, specific or class

(PABP (poly(A)-binding protein); methods of

detg. individual hypersensitivity to a pharmaceutical

agent from gene expression profile)

IT Proteins, specific or class

(PDGF assocd. protein; methods of detg.

individual hypersensitivity to a pharmaceutical agent from gene expression profile)

IT Proteins, specific or class

(c-myc binding protein; methods of detg.

individual hypersensitivity to a pharmaceutical agent from gene expression profile)

IT Gene, animal

(lipopolysaccharide binding protein; methods of

detg. individual hypersensitivity to a pharmaceutical
agent from gene expression profile)

IT APC protein

(methods of **detg**. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

IT Mdm2 protein

(methods of **detg**. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

IT Multidrug resistance proteins

(methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

IT Myelin basic protein

(methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

IT Prion proteins

(methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

IT p53 (protein)

(methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

IT Gene, animal

(myelin basic protein; methods of detg.

individual hypersensitivity to a pharmaceutical agent from gene expression profile)

IT Gene, animal

(nucleic acid binding protein; methods of detg

. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

IT Proteins, specific or class

(oxysterol binding protein; methods of detg.

individual hypersensitivity to a pharmaceutical agent from gene

expression profile) ΙT Proteins, specific or class (pancreatitis-assocd. protein; methods of detg . individual hypersensitivity to a pharmaceutical agent from gene expression profile) ΙT Proteins, general, biological studies (proteinuria; methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile) ΙT Proteins, specific or class (thiol-specific antioxidant protein; methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile) ΙΤ Proteins, specific or class (ts11 gene encoding G1 progression protein; methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile) ΙT 50-02-2, Dexamethasone 50-06-6, Phenobarbital, biological studies 50-18-0, Cyclophosphamide 50-23-7, Hydrocortisone Prednisolone 50-28-2, Estradiol, biological studies 50-44-2, 50-48-6, Amitriptyline 6-Thiopurine 50-55-5, Reserpine 50-76-0, Actinomycin D 50-78-2, Aspirin 51-06-9, Procainamide 51-21-8, Fluorouracil 51-34-3, Scopolamine 51-48-9, Levothyroxine, biological studies 51-49-0, Dextrothyroxine 51-55-8, Atropine, biological studies 51-75-2, Mechlorethamine 52-01-7, Spironolactone 52-53-9, Verapamil 52-67-5. Penicillamine 52-86-8, Haloperidol 53-03-2, Prednisone 53-06-5, Cortisone 53-19-0, Mitotane 53-33-8, Paramethasone 53-86-1, Indomethacin 54-05-7, Chloroquine 54-11-5, Nicotine 54-31-9, Furosemide 54-36-4, Metyrapone 54-85-3, Isoniazid 55-63-0, Nitroglycerin 55-65-2, Guanethidine 55-98-1, Busulfan 56-54-2, Quinidine 56-75-7, Chloramphenicol 57-22-7, Vincristine 57-41-0, Phenytoin 57-53-4, Meprobamate 57-63-6, Ethinyl 57-66-9, Probenecid 57-83-0, Progestin, biological estradiol studies 57-96-5, Sulfinpyrazone 58-05-9, Leucovorin Pyrimethamine 58-32-2, Dipyridamole 58-39-9, Perphenazine 58-54-8, Ethacrynic acid 58-55-9, Theophylline, biological studies 58-61-7, Adenosine, biological studies 58-74-2, Papaverine 58-93-5, Hydrochlorothiazide 58-94-6, Thiazide 59-05-2, Methotrexate 59-42-7, Phenylephrine 59-43-8, Thiamine, 59-92-7, Levodopa, biological studies biological studies 59-99-4, Neostigmine 60-40-2, Mecamylamine 60-54-8, Tetracycline 60-79-7, Ergonovine 60-87-7, Promethazine 61-32-5, Methicillin

61-72-3, Cloxacillin 64-75-5, Tetracycline hydrochloride

studies 68-22-4D, Norethindrone, mixt. with ethinyl estradiol

65-23-6, Pyridoxine

66-97-7, Psoralen 67-20-9, Nitrofurantoin

67-68-5, Dimethyl sulfoxide, biological

64-77-7, Tolbutamide 64-86-8, Colchicine

66-79-5, Oxacillin

67-45-8, Furazolidone

68-41-7, Cycloserine 68-88-2, Hydroxyzine 69-53-4, Ampicillin 69-72-7, biological studies 69-89-6, Xanthine 73 - 24 - 5, 6-Aminopurine, biological studies 73-31-4, Melatonin 76-57-3, Codeine 77-09-8, Phenolphthalein Oxycodone 77-19-0, Dicyclomine 77-36-1, Chlorthalidone 78-44-4, Carisoprodol 80-08-0, Dapsone 81-23-2, Dehydrocholic acid 81-81-2, Warfarin 82-92-8, Cyclizine 82-95-1, Buclizine 83-43-2, Methylprednisolone 83-73-8, Iodoquinol 83-89-6, Quinacrine 83-98-7, Orphenadrine 86-54-4, Hydralazine 89-57-6, Mesalamine 90-34-6, Primaguine 90-82-4, Pseudoephedrine 91-64-5, Coumarin 92-13-7, Pilocarpine 92-84-2, Phenothiazine 93-14-1, Guaifenesin 94-20-2, Chlorpropamide 94-36-0, Benzoyl peroxide, biological studies 94-78-0, Phenazopyridine 95-25-0, Chlorzoxazone 96-64-0, Soman 97-77-8, Disulfiram 99-66-1, Valproic acid 100-33-4, Pentamidine 100-97-0, Methenamine, biological studies 101-31-5, Hyoscyamine 103-90-2, Acetaminophen 113-18-8, Ethchlorvynol 113-42-8, Methylergonovine 113-45-1, Methylphenidate 114-07-8, Erýthromycin 114-86-3, Phenformin 118-42-3, Hydroxychloroguine 122-09-8, Phentermine Succinimide 123-63-7, Paraldehyde 124-94-7, Triamcinolone 125-29-1, Hydrocodone 125-33-7, Primidone 125-64-4, Methyprylon 125-71-3, Dextromethorphan 125-84-8, Aminoglutethimide 126-07-8. Griseofulvin 126-52-3, Ethinamate 127-07-1, Hydroxyurea 127-69-5, Sulfisoxazole 128-13-2, Ursodiol 130-95-0, Quinine 132-17-2, Benztropine 133-10-8, Sodium p-aminosalicylate 137-58-6, Lidocaine 138-56-7, Trimethobenzamide 147-94-4, AraC Trihexyphenidyl 147-52-4, Nafcillin 148-82-3, Melphalan 154-21-2, Lincomycin 154-42-7, Thioguanine 154-93-8, 155-97-5, Pyridostigmine Carmustine 298-46-4, 5H-Dibenz[b,f]azepine-5-carboxamide 298-50-0, Propantheline 299-42-3, Ephedrine 300-62-9D, Amphetamine, mixed 300-62-9D, Amphetamine, mixed salts 302-17-0, Chloral hydrate 302-79-4, Tretinoin 303-53-7, Cyclobenzaprine 305-03-3, 315-30-0, Allopurinol 321-64-2, Tacrine Chlorambucil 361-37-5, Methysergide 363-24-6, Dinoprostone Polythiazide 364-62-5, Metoclopramide 378-44-9, Betamethasone 389-08-2, Nalidixic acid 395-28-8, Isoxsuprine 439-14-5, Diazepam 443-48-1, Metronidazole 446-86-6, Azathioprine 456-59-7, Cyclandelate 461-72-3, Hydantoin 463-04-7, Amyl nitrite 469-62-5, Propoxyphene 474-25-9, Chenodiol 480-30-8, Dichloralphenazone 484-23-1, Dihydralazine 503-01-5, Isometheptene 512-15-2, Cyclopentolate 520-85-4, Medroxyprogesterone 525-66-6, Propranolol 526-36-3, Xylometazoline 536-33-4, Ethionamide 541-15-1, Levocarnitine 546-88-3, Acetohydroxamic acid 555-30-6, Methyl dopa 564-25-0, Doxycycline 569-65-3, Meclizine 577-11-7, Docusate sodium 596-51-0, Glycopyrrolate 599-79-1, Sulfasalazine Bisacodyl 634-03-7, Phendimetrazine 637-07-0, Clofibrate

657-24-9, Metformin 671-16-9, Procarbazine 672-87-7, Metyrosine 674-38-4, Bethanechol 723-46-6, Sulfamethoxazole 738-70-5, 745-65-3, Alprostadil 791-35-5, Chlophedianol Trimethoprim 797-63-7, Levonorgestrel 797-64-8D, L-Norgestrel, ethinyl 846-49-1, Lorazepam 846-50-4, Temazepam estradiol mixt. 911-45-5, Clomiphene 915-30-0, Diphenoxylate 962-58-3, Diazoxon 968-93-4, Testolactone 972-02-1, Diphenidol 990-73-8, Fentanyl citrate 1134-47-0, Baclofen 1143-38-0, Anthralin 1321-13-7, Potassium aminobenzoate 1397-89-3, Amphotericin B 1400-61-9, Nystatin 1404-04-2, Neomycin 1404-04-2D, Neomycin, mixt. with 1404-90-6, Vancomycin 1406-05-9, Penicillin polymx/HC 1491-59-4, Oxymetazoline 1622-61-3, Clonazepam 1953-02-2, 1977-10-2, Loxapine 2152-34-3, Pemoline 2152-44-5, Betamethasone valerate 2447-57-6, Sulfadoxine 2451-01-6, Terpin 2609-46-3, Amiloride 2809-21-4 2998-57-4, Estramustine hydrate 3116-76-5, Dicloxacillin 3313-26-6, Thiothixene 3385-03-3, 3485-14-1, Cyclacillin 3737-09-5, Disopyramide Flunisolide 3778-73-2, Iphosphamide 3930-20-9, Sotalol 4205-90-7, Clonidine 4419-39-0, Beclomethasone

(methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile) 107-97-1, Sarcosin 447-41-6, Nylidrin 8056-51-7 9000-86-6, Alanine aminotransferase 9000-97-9 9001-05-2, Catalase 9001-40-5, Glucose-6-phosphate dehydrogenase 9001-48-3, Glutathione reductase 9001-50-7, Glyceraldehyde 3-phosphate 9001-62-1, Hepatic lipase 9001-84-7, Phospholipase dehydrogenase 9002-03-3, Dihydrofolate reductase 9002-06-6, Thymidine 9002-12-4, Urate oxidase 9002-67-9, Luteinizing hormone kinase 9003-99-0, Myeloperoxidase 9012-25-3, Catechol-O-methyltransferase 9012-38-8, PAPS synthetase 9012-39-9 9012-52-6, S-Adenosylmethionine synthetase 9013-08-5, Phosphoenolpyruvate carboxykinase 9013-18-7, Fatty acyl-CoA synthetase 9013-38-1, Dopamine .beta.-hydroxylase 9013-66-5, Glutathione peroxidase 9013-79-0, Neuropathy target esterase 9014-55-5, Tyrosine 9015-71-8, Corticotropin releasing hormone aminotransferase 9015-81-0, 17-.beta. Hydroxysteroid dehydrogenase 9016-12-0, Hypoxanthine-guanine phosphoribosyltransferase 9023-44-3, Tryptophanyl-tRNA synthetase 9023-62-5, Glutathione synthetase 9023-64-7, .gamma.-Glutamylcysteinyl synthetase 9023-70-5, Glutamine synthetase 9024-60-6, Ornithine decarboxylase 9024-61-7, Histidine decarboxylase 9025-32-5, Prolidase 9026-00-0, Cholesterol esterase 9026-09-9, Phenol sulfotransferase 9026-43-1, Serine kinase 9026-51-1, Nucleoside diphosphate kinase 9027-13-8, Enoyl-CoA hydratase 9027-65-0, Acyl-CoA dehydrogenase 9028-06-2 9028-31-3, Aldose reductase 9028-35-7, HMG COA reductase 9028-41-5, Hydroxyacyl-Coenzyme A dehydrogenase 9028-86-8, Aldehyde dehydrogenase 9029-73-6, Phenyl alanine hydroxylase 9029-80-5, Histamine N-methyltransferase 9029-97-4,

ΙT

3-Ketoacyl-CoA thiolase 9031-37-2, Ceruloplasmin 9031-54-3, 9031-61-2, Thymidylate synthase Sphingomvelinase 9031-72-5, Alcohol dehydrogenase 9032-20-6, DT-Diaphorase 9035-58-9, Blood-coagulation factor III 9036-22-0, Tyrosine hydroxylase 9037-21-2, Tryptophan hydroxylase 9037-62-1, Glycyl tRNA 9039-06-9, NADPH cytochrome P450 reductase synthetase 9040-57-7. 9041-92-3 9045-77-6, Fatty acid Ribonucleotide reductase 9046-27-9, .gamma.-Glutamyl transpeptidase 9048-63-9, Epoxide hydrolase 9055-67-8, Poly(ADP-ribose)polymerase 9059-25-0, Lysyl oxidase 9068-41-1, Carnitine palmitoyltransferase 9074-02-6, Malic enzyme 9074-10-6, Biliverdin reductase 9074-19-5, Hydratase 9074-87-7, .gamma.-Glutamyl hydrolase 9081-36-1, 25-Hydroxyvitamin D3 1-hydroxylase 11096-26-7, Erythropoietin 37205-63-3, ATP synthase 37237-44-8, Glucosylceramide synthase 37289-06-8, Acid ceramidase 37292-81-2, Cytochrome p 450 11A1 37318-49-3, Protein 39391-18-9, Prostaglandin H synthase **disulfide** isomerase 52228-01-0 56093-23-3, .alpha.-1,2-Fucosyl transferase 56645-49-9, Cathepsin G 59536-73-1, Phosphomannomutase 59536-74-2, Very long-chain acyl-CoA dehydrogenase 60267-61-0, Ubiquitin 60616-82-2, Cathepsin L 61116-22-1, Fatty acyl-CoA 62229-50-9, Epidermal growth factor oxidase 67339-09-7, Thiopurine methyltransferase 67763-96-6, Insulin-like growth factor 1 67763-97-7, Insulin-like growth factor II 77271-19-3, 6-O-Methylguanine-DNA methyltransferase 77847-96-2, Prostacyclin-stimulating factor 79747-53-8, Protein tyrosine 79955-99-0, Stromelysin-1 phosphatase 80146-85-6, Tissue Transglutaminase 80295-41-6, Complement component C3 81627-83-0, Colony stimulating factor -1 82391-43-3, 12-Lipoxygenase 83869-56-1, Granulocyte-macrophage colony-stimulating 83268-44-4 85637-73-6, Atrial natriuretic factor 87397-91-9, factor Thymosin .beta.10 88943-21-9, Proteinase .alpha.1-inhibitor III 89964-14-7, Prothymosin, alpha 90698-26-3, Ribosomal protein S6 96024-44-1, Granulin 105238-46-8, Macropain 106096-92-8, Fibroblast growth factor, acidic 106956-32-5, Oncostatin M 112130-98-0, Procathepsin L 114949-22-3, Activin (117698-12-1, Paraoxonase 119418-04-1, Galanin 122191-40-6, Caspase-1 123626-67-5, Endothelin-1 125978-95-2, Nitric oxide synthase 127464-60-2, Vascular endothelial growth 137632-07-6, Extracellular-signal-regulated kinase 1 138238-81-0, Endothelin converting enzyme-1 140208-24-8, Tissue inhibitor of metalloproteinase-1 141176-92-3 141349-86-2, Cyclin dependent kinase 2 141436-78-4, Protein kinase C 142243-03-6, Plasminogen activator inhibitor 2 142805-56-9, DNA topoisomerase 142805-58-1, MAP kinase kinase 143180-75-0, DNA topoisomerase 143375-65-9, Cyclin dependent kinase 1 145809-21-8, Tissue inhibitor of metalloproteinase-3 146480-35-5, Matrix metalloproteinase-2 147014-97-9, Cyclin dependent kinase 4

148348-15-6, Fibroblast growth factor 7 149316-81-4, Branched chain acyl-CoA oxidase 149371-05-1, Kinase (phosphorylating), gene c-abl protein 149885-78-9, Hepatocyte growth factor 154907-65-0, Checkpoint kinase 155807-64-0, FEN-1 activator Endonuclease 165245-96-5, p38 Mitogen-activated protein kinase 169592-56-7, CPP32 **proteinase** 179241-70-4, Protein kinase ZPK 179241-78-2, Caspase 8 182372-14-1, Caspase 2 182372-15-2, Caspase 6 182762-08-9, Caspase 4 189258-14-8, 192465-11-5, Caspase 5 193363-12-1, Vascular endothelial growth factor D 194554-71-7, Tissue factor pathway inhibitor 205944-50-9, Osteoprotegerin 220983-94-8, Sorbitol dehydrogenase 289898-51-7, JNK1 protein kinase 303752-61-6, DNA dependent protein kinase 329736-03-0, Cytochrome p450 3A4 329764-85-4, Cytochrome p450 1A1 329900-75-6, Cyclooxygenase 2 329978-01-0, Cytochrome p450 2C9 330196-64-0, Cytochrome p450 1A2 330196-93-5, Cytochrome p450 2E1 330207-10-8, Cytochrome p450 2B1 330589-90-7, Cytochrome p450 2C19 330596-22-0, Cytochrome p450 1B1 330597-62-1, Cytochrome p450 2D6 330975-22-9, Macrostatin 331462-97-6, Cytochrome p450 2B2 331462-98-7, Cytochrome p450 3A1 331823-00-8, Cytochrome p450 2C11 331823-12-2, Cytochrome p450 2C12 331823-27-9, Cytochrome p450 2A1 331827-06-6, Cytochrome 332847-52-6, Cytochrome p450 4A 336884-26-5, Cytochrome p450 2B10 338964-08-2, P 450 17A 338969-62-3, P 450 2A3 338969-69-0, P 450 2F2 338969-71-4, P 450 4A1 (methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

L98 ANSWER 16 OF 28 HCA COPYRIGHT 2004 ACS on STN

131:269143 Dynamic measurement of myosin light-chain-domain tilt and twist in muscle contraction. Corrie, J. E. T.; Brandmeier, B. D.; Ferguson, R. E.; Trentham, D. R.; Kendrick-Jones, J.; Hopkins, S. C.; Van Der Heide, U. A.; Goldman, Y. E.; Sabido-David, C.; Dale, R. E.; Criddle, S.; Irving, M. (National Institute for Medical Research, London, NW7 1AA, UK). Nature (London), 400(6743), 425-430 (English) 1999. CODEN: NATUAS. ISSN: 0028-0836. Publisher: Macmillan Magazines.

AB A new method is described for measuring motions of protein domains in their native environment on the physiol. timescale. Pairs of cysteines are introduced into the domain at sites chosen from its static structure and are crosslinked by a bifunctional rhodamine. Domain orientation in a reconstituted macromol. complex is detd. by combining fluorescence polarization data from a small no. of such labeled cysteine pairs. This approach bridges the gap between in vitro studies of protein structure and cellular studies of protein function and is used here to measure the tilt and twist of the myosin light-chain domain with respect to actin filaments in single muscle cells. The results reveal the structural basis for the

lever-arm action of the light-chain domain of the myosin motor during force generation in muscle.

IT 203580-70-5

(bifunctional rhodamine label for myosin light-chain-domain; dynamic measurement of myosin light-chain-domain tilt and twist in muscle contraction)

RN 203580-70-5 HCA

CN Acetamide, N,N'-[(3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthene]-3',6'-diyl)bis[(methylimino)-2,1-ethanediyl]]bis[2-iodo-(9CI) (CA INDEX NAME)

CC 9-5 (Biochemical Methods)

Section cross-reference(s): 6, 13

IT Quaternary structure

(protein; dynamic measurement of myosin light-chain-domain tilt and twist in muscle contraction)

IT 203580-70-5

(bifunctional rhodamine label for myosin light-chain-domain; dynamic measurement of myosin light-chain-domain tilt and twist in muscle contraction)

L98 ANSWER 17 OF 28 HCA COPYRIGHT 2004 ACS on STN

131:167851 Purification, structural characterization, cloning and immunocytochemical localization of chemoreception proteins from Schistocerca gregaria. Angeli, Sergio; Ceron, Francesca; Scaloni, Andrea; Monti, Maria; Monteforti, Gaia; Minnocci, Antonio; Petacchi, Ruggero; Pelosi, Paolo (Scuola Superiore di Studi Universitari e di Perfezionamento "S. Anna", Pisa, Italy). European Journal of Biochemistry, 262(3), 745-754 (English) 1999. CODEN: EJBCAI. ISSN: 0014-2956. Publisher: Blackwell Science Ltd..

AB Sol. low-mol.-mass protein isoforms were purified from chemosensory organs (antennae, tarsi, and labrum) of the desert locust S. gregaria. Five genes encoding proteins of this group were amplified by PCR from cDNAs of tarsi and sequenced. Their expression products are polypeptide chains of 109 amino acids showing 40-50%

sequence identity with putative olfactory proteins from Drosophila melanogaster and Cactoblastis cactorum. Direct structural investigation on isoforms purified from chemosensory organs revealed the presence in the expression products of two of the genes cloned. Two addnl. protein isoforms were detected and their mol. structure exhaustively characterized. MS anal. of all isoforms demonstrated that the 4 cysteine residues conserved in the polypeptide chain were involved in disulfide bridges (Cys29-Cys38 and Cys57-Cys60) and indicated the absence of any addnl. post-translational modifications. Immunocytochem. expts., performed with rabbit antiserum raised against the protein isoform mixt., showed selective labeling of the outer lymph in contact sensilla of tarsi, maxillary palps, and antennae. Other types of sensilla were not labeled, nor were the cuticle and dendrites of the sensory cells. No binding of radioactively labeled glucose or bicarbonate was detected, in disagreement with the hypothesis that this class of proteins is involved in the CO2-sensing cascade. Our exptl. data suggest that the proteins described here could be involved in contact chemoreception in Orthoptera.

CC 12-1 (Nonmammalian Biochemistry) Section cross-reference(s): 3, 6

ANSWER 18 OF 28 HCA COPYRIGHT 2004 ACS on STN L98 131:56155 Methods for the simultaneous identification of novel biological targets and lead structures for drug development using combinatorial libraries and probes. Heefner, Donald L.; Zepp, Charles M.; Gao, Yun; Jones, Steven W. (Sepracor Inc., USA). PCT Int. Appl. WO 9931267 A1 19990624, 125 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). APPLICATION: WO 1998-US26894 19981218. PIXXD2. PRIORITY: US 1997-68035 19971218.

The combinatorial screening assays and detection methods of the present invention encompass highly diversified libraries of compds. which act as fingerprints to allow for the identification of specific mol. differences existing between biol. samples. The combinatorial screening assay and detection methods of the present invention utilize highly diversified libraries of compds. to interrogate and characterize complex mixts. in order to identify specific mol. differences existing between biol. samples, which may serve as targets for diagnosis of development of therapeutics. The invention is base, in part, on the design of sensitive, rapid,

homogeneous assay systems that permit the evaluation, interrogation, and characterization of samples using complex, highly diversified libraries of mol. probes. The ability to run the high throughput assays in a homogeneous format increases sensitivity of screening. In addn., the homogeneous format allows the mols. which interact to maintain their native or active conformations. Moreover, the homogeneous assay systems of the invention utilize robust detection systems that do not require sepn. steps for detection of reaction products. The assays of the invention can be used for diagnostics, drug screening and discovery, target-driven discover, and in the field of proteomics and genomics for the identification of disease markers and drug targets.

IT 220518-50-3, Fim-1

(identification of novel biol. targets and lead structures for drug development using combinatorial libraries and probes)

RN 220518-50-3 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-5-carboxamide, N-[3-[3-[2,5-dihydro-4-(1-methyl-1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]-1H-indol-1-yl]propyl]-3',6'-dihydroxy-3-oxo-(9CI) (CA INDEX NAME)

IC ICM C12Q001-00

ICS C12Q001-68; C12Q001-70; G01N033-53; G01N033-566; G01N033-567; G01N021-00; G01N021-76

CC 9-16 (Biochemical Methods)
Section cross-reference(s): 1, 6, 13, 14

ΙΤ Animal tissue Autoimmune disease Biochemical molecules Blood Blood analysis Blood plasma Blood serum Body fluid Cell Chemiluminescence spectroscopy Chemiluminescent substances Chicken (Gallus domesticus) Combinatorial chemistry Combinatorial library Crosslinking Diabetes mellitus Diagnosis Disease, animal Drug design Drug screening Drugs Epitopes Erythrocyte Escherichia coli Fluorescent dyes Fluorescent probes Fluorescent substances Fluorometry Heart, disease Immobilization, biochemical Infection Inflammation Leukocyte Lymph Microorganism Molecules Neoplasm Photochemistry Polarized fluorescence Radioactive substances Scintillators Test kits Therapy Toxicity Urine Urine analysis Virus

(identification of novel biol. targets and lead structures for

drug development using combinatorial libraries and probes) ΙT Amino acids, analysis Antibodies Antigens Carbohydrates, analysis Chemokines Cytokines DNA Enzymes, analysis Glycolipids Glycoproteins, general, analysis Growth factors, animal Inorganic compounds Ligands Lipids, analysis Lipopolysaccharides Lipoproteins Nucleosides, analysis Nucleotides, analysis Oligonucleotides Oligosaccharides, analysis Organic compounds, analysis Peptides, analysis Polymers, analysis Polynucleotides Polysaccharides, analysis Proteins, general, analysis RNA Receptors (identification of novel biol. targets and lead structures for drug development using combinatorial libraries and probes) IT 50-06-6D, Phenobarbital, reaction products with fluorescein 50-67-9D, Serotonin, reaction products with coumarin, analysis 57-41-0D, Phenytoin, reaction products with fluorescein 58-55-9D, Theophylline, reaction products with fluorescein 70-51-9D, Desferrioxamine, reaction products with fluorescein 125-33-7D, Primidone, reaction products with fluorescein 536-21-0D, Norphenylephrine, reaction products with coumarin 1403-66-3D, Gentamicin, reaction products with fluorescein 1404-90-6D, Vancomycin, reaction products with fluorescein 1446-61-3D. Dehydroabietylamine, reaction products with fluorescein and coumarin 6621-47-2D, Perhexiline, reaction products with fluorescein 11032-79-4D, .alpha.-Bungarotoxin, reaction products with FITC 20350-15-6D, Brefeldin A, reaction products with BODIPY 32231-06-4D, 1-Piperonylpiperazine, reaction products with fluorescein and coumarin 32795-44-1D, N-Acetylprocainamide, reaction products with fluorescein 32986-56-4D, Tobramycin, reaction products with fluorescein 37517-28-5D, Amikacin, reaction

products with fluorescein 66580-68-5D, Globotriose, reaction products with fluorescein 70458-96-7D, Norfloxacin, reaction products with coumarin 74011-58-8D, Enoxacin, reaction products 84031-84-5, Colchicine fluorescein with coumarin 87134-87-0 88641-41-2, Naloxone fluorescein 88641-43-4 107827-77-0 121086-10-0, BODIPY FL-NAPS 121714-22-5, Fluo-3AM 134759-22-1, Fluorescein biotin 135243-34-4, BODIPY FL PPHT 137759-83-2 151736-99-1, Cholesteryl-BODIPY FL C12 138777-24-9, C 8FDG 170516-42-4, Phen Green 168004-84-0 175799-93-6, BODIPY 195244-55-4, Sodium Green 197460-05-2, Fluorescein FL-prazosin methotrexate 212116-60-4, BODIPY FL-forskolin 216483-91-9, Ro 216483-92-0, BODIPY FL-amiloride 1986-BODIPY 216571-97-0, BODIPY FL-ABT 216571-98-1, BODIPY FL-bisindolylmaleimide 216571-99-2, BODIPY FL-thapsigargin 216572-00-8, BODIPY FL-X ryanodine 216854-76-1, Dexamethasone fluorescein 217189-42-9, (+)-DM-BODIPY dihydropyridine 217189-43-0, (-)-DM-BODIPY dihydropyridine 217189-44-1, BODIPY FL C12-galactocerebroside 220518-50-3, Fim-1 228111-69-1 228111-70-4 228111-71-5 228262-70-2, 228265-61-0, BODIPY FL pirenzepine Fluorescein DHPE 228265-62-1, BODIPY FL-CGP 12177 228265-63-2, BODIPY FL C12-MPP 228265-94-9, 288374-37-8, Newport Green BODIPY FL-Sch 23390 (identification of novel biol. targets and lead structures for drug development using combinatorial libraries and probes)

L98 ANSWER 19 OF 28 HCA COPYRIGHT 2004 ACS on STN 130:308804 Target protein sequences for binding of synthetic biarsenical Tsien, Roger Y.; Griffin, Albert B. (The Regents of the molecules. University of California, USA). PCT Int. Appl. WO 9921013 A1 19990429, 77 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US22363 19981021. PRIORITY: US 1997-955050 19971021; US 1997-955206 19971021; US 1997-955859 19971021. AB The present invention features biarsenical mols. and target sequences that specifically react with the biarsenical mols.

AB The present invention features biarsenical mols. and target sequences that specifically react with the biarsenical mols. A bonding partner comprises a carrier polypeptide and a target sequence, wherein the target sequence is heterologous to the carrier polypeptide and the target sequence contains one or more cysteines capable of specifically reacting with a biarsenical mol. Bonding partners that include target sequences, vectors that include nucleic acid sequences that encode the target sequences and host cells that include the target sequences are also featured in the invention. One example of a biarsenical compd. is

an arsenical deriv. of fluorescein.

IT 52-90-4, L-Cysteine, biological studies

(target protein sequences for binding of synthetic biarsenical mols.)

RN 52-90-4 HCA

CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 223673-80-1 223673-81-2 223673-82-3

(target protein sequences for binding of synthetic biarsenical mols.)

RN 223673-80-1 HCA

CN 1,4-Benzenedicarboxylic acid, 2,5-bis[4,5-bis(1,3,2-dithiarsolan-2-yl)-3,6-dihydroxy-9H-xanthen-9-yl]- (9CI) (CA INDEX NAME)

RN 223673-81-2 HCA

CN 1,3-Benzenedicarboxylic acid, 4,6-bis[4,5-bis(1,3,2-dithiarsolan-2-yl)-3,6-dihydroxy-9H-xanthen-9-yl]- (9CI) (CA INDEX NAME)

RN 223673-82-3 HCA

CN 9H-Xanthene-9-propanamide, N,N'-1,3-propanediylbis[4,5-bis(1,3,2-dithiarsolan-2-yl)-3,6-dihydroxy- (9CI) (CA INDEX NAME)

IT 223673-84-5

(target protein sequences for binding of synthetic biarsenical mols.)

RN 223673-84-5 HCA

CN 1,4-Benzenedicarboxylic acid, 2,5-bis(3,6-dihydroxy-9H-xanthen-9-yl)-

(9CI) (CA INDEX NAME)

IT 223673-86-7P

(target protein sequences for binding of synthetic biarsenical mols.)

RN 223673-86-7 HCA

CN Mercurate(2-), tetrakis(acetato-.kappa.O)[.mu.-[(2,5-dicarboxylato-1,4-phenylene)bis(3,6-dihydroxy-9H-xanthene-9,4,5-triyl)]]tetra-, dihydrogen (9CI) (CA INDEX NAME)

OH

$$C = Hg = 0$$
 $C = Hg = 0$
 $C = Hg = 0$

- IC ICM G01N033-566
 - ICS C07F009-80; C12N015-09; C12N015-64
- CC 9-15 (Biochemical Methods)
 - Section cross-reference(s): 6
- IT Peptides, analysis
 - Proteins, specific or class
 - (labeled; target **protein** sequences for binding of synthetic biarsenical mols.)
- IT Calmodulins
 - Peptides, analysis
 - Proteins, general, analysis
 - (target **protein** sequences for binding of synthetic biarsenical mols.)
- IT 52-90-4, L-Cysteine, biological studies
 - (target protein sequences for binding of synthetic biarsenical mols.)
- IT 223673-80-1 223673-81-2 223673-82-3
 - (target protein sequences for binding of synthetic biarsenical mols.)
- TT 76-54-0, 2',7'-Dichlorofluorescein 89-05-4, 1,2,4,5-Benzenetetracarboxylic acid 108-46-3, 1,3-Benzenediol, reactions 540-63-6, 1,2-Ethanedithiol 1600-27-7, Mercuric acetate 7784-34-1, Arsenic trichloride 32382-27-7, Fluorescein mercuric acetate 223673-84-5
 - (target protein sequences for binding of synthetic biarsenical mols.)
- IT 54210-30-9P **223673-86-7P** 223673-87-8P
 - (target protein sequences for binding of synthetic biarsenical mols.)
- L98 ANSWER 20 OF 28 HCA COPYRIGHT 2004 ACS on STN
- 130:264438 Sulfonated xanthene derivatives synthesis and applications as fluorescent stains. Mao, Fei; Leung, Wai-Yee; Haugland, Richard P. (Molecular Probes, Inc., USA). PCT Int. Appl. WO 9915517 A1 19990401, 63 pp. DESIGNATED STATES: W: AU, CA, JP, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US19921 19980923. PRIORITY: US 1997-935963 19970923.
- AB The present invention describes xanthene dyes, including rhodamines, rhodols and fluoresceins that are substituted one or more times by a sulfonic acid or a salt of a sulfonic acid. The dyes of the invention, including chem. reactive dyes and dye-conjugates are useful as fluorescent probes, particularly in biol. samples.
- IT 9003-53-6DP, Polystyrene, amine deriv.
 - (fluorescently labeled microspheres; sulfonated xanthene derivs. synthesis and applications as fluorescent stains)
- RN 9003-53-6 HCA
- CN Benzene, ethenyl-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 100-42-5 CMF C8 H8

 $H_2C = CH - Ph$

IT 222165-01-7P 222165-02-8P

(sulfonated xanthene derivs. synthesis and applications as fluorescent stains)

RN 222165-01-7 HCA

CN Pyrano[3,2-g:5,6-g']diquinolin-13-ium, 6-[2-carboxy-4(or 5)-[[5-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)pentyl]amino]carbonyl]phenyl]-1,2,10,11-tetrahydro-1,2,2,10,10,11-hexamethyl-4,8-bis(sulfomethyl)-, inner salt, monosodium salt (9CI) (CA INDEX NAME)

Na

RN 222165-02-8 HCA

CN Xanthylium, 3,6-diamino-9-[2-carboxy-4(or 5)-[[[5-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)pentyl]amino]carbonyl]phenyl]-4,5-disulfo-, inner salt, sodium salt (9CI) (CA INDEX NAME)

🖜x Na

IT 222159-86-6P 222165-01-7DP, conjugate

(sulfonated xanthene derivs. synthesis and applications as fluorescent stains)

RN 222159-86-6 HCA

CN Pyrano[3,2-g:5,6-g']diquinolin-13-ium, 6-[2-carboxy-4-[[[[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]amino]carbonyl]phenyl]-1,2,10,11-tetrahydro-1,2,2,10,10,11-hexamethyl-4,8-bis(sulfomethyl)-, inner salt, monolithium salt (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

• Li

RN 222165-01-7 HCA
CN Pyrano[3,2-g:5,6-g']diquinolin-13-ium, 6-[2-carboxy-4(or 5)-[[[5-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)pentyl]amino]carbonyl]phenyl]-1,2,10,11-tetrahydro-1,2,2,10,10,11-hexamethyl-4,8-bis(sulfomethyl)-, inner salt, monosodium salt (9CI) (CA INDEX NAME)

Na

IC ICM C07D311-82

ICS C07D491-14; C07D405-12; C07D491-22; C07H003-06; C07H021-00; C07H019-04; C07K014-415; G01N001-30

CC 9-15 (Biochemical Methods)

Section cross-reference(s): 6, 27

IT Proteins, specific or class

(A; sulfonated xanthene derivs. synthesis and applications as fluorescent stains)

IT Immunoglobulins

Proteins, specific or class

(G; sulfonated xanthene derivs. synthesis and applications as fluorescent stains)

IT Phycoerythrins

(R-phycoerythrins, pyridyldisulfide modified;

sulfonated xanthene derivs. synthesis and applications as fluorescent stains)

IT Proteins, specific or class

(conjugates, sulfonated xanthene conjugate; sulfonated xanthene derivs. synthesis and applications as fluorescent stains)

IT Actins

Agglutinins and Lectins

Allophycocyanins

Amino acids, biological studies

Antibodies

Avidins

IT

ΤТ

ΙΤ

ΙΤ

ΙΤ

Biliproteins Disaccharides Growth factors, animal Haptens Lipids, biological studies Monosaccharides Nucleic acids Nucleotides, biological studies Peptides, biological studies Polymers, biological studies Polysaccharides, biological studies Toxins (sulfonated xanthene conjugate; sulfonated xanthene derivs. synthesis and applications as fluorescent stains) Protein receptors (sulfonated xanthene derivs. synthesis and applications as fluorescent stains) Proteins, general, analysis (sulfonated xanthene derivs. synthesis and applications as fluorescent stains) 9003-53-6DP, Polystyrene, amine deriv. (fluorescently labeled microspheres; sulfonated xanthene derivs. synthesis and applications as fluorescent stains) 222159-72-0P 222159-73-1P 222159-74-2P 222159-70-8P 222159-84-4P 222159-85-5P 222159-79-7P 222159-82-2P 222164-80-9P 222164-81-0P 222164-92-3P 222164-95-6P 222164-98-9P 222164-99-0P **222165-01-7P 222165-02-8P** 222165-04-0P (sulfonated xanthene derivs. synthesis and applications as fluorescent stains) 2321-07-5DP, Fluorescein, conjugates 146397-20-8DP, CY-3, conjugates 183185-51-5DP, Rhodol Green, conjugates 189200-71-3DP, Rhodamine Green, conjugates 199745-67-0DP, Texas 222159-76-4P 222159-78-6P Red-X, conjugates 222159-80-0P 222159-82-2DP, conjugate 222159-83-3P 222159-81-1P 222159-92-4DP, conjugate 222159-93-5DP, 222159-86-6P 222164-83-2P 222164-86-5DP, conjugate 222164-82-1P conjugate 222164-87-6P 222164-88-7P 222164-91-2P 222164-92-3DP, conjugate 222164-93-4P 222164-95-6DP, conjugate 222165-00-6P **222165-01-7DP**, conjugate 222165-04-0DP, spiperone conjugate (sulfonated xanthene derivs. synthesis and applications as fluorescent stains)

L98 ANSWER 21 OF 28 HCA COPYRIGHT 2004 ACS on STN
130:135555 Determination of the **disulfide** bonds within a B
domain variant surface glycoprotein from Trypanosoma congolense.

Bussler, Holm; Linder, Monica; Linder, Dietmar; Reinwald, Erwin (Biochemisches Institut am Klinikum, Justus-Liebig-Universitat, Giessen, 35392, Germany). Journal of Biological Chemistry, 273(49), 32582-32586 (English) 1998. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology. The disulfide bonds within a variant surface glycoprotein AΒ from Trypanosoma congolense have been detd. L-[35S]Cysteine metabolically labeled protein was digested with trypsin, and radiolabeled peptides were sepd. by reversed-phase high performance liq. chromatog., and putative cystine-contg. peptides were subdigested with other proteases and analyzed after further purifn. by amino acid sequencing and mass spectrometry. All eight cysteine residues of the protein, located within the N-terminal domain, are covalently linked. disulfide bonds are between cysteines 16/236, 171/193, 195/206, and 286/298. This is, for the first time, the detn. of disulfide bonds within a variant surface glycoprotein belonging to the B-type. As all the eight cysteines of BENat 1.3 variant surface glycoprotein are positionally conserved, the cystine pattern of this protein can be regarded as a prototype of disulfide bonding within B-type variant surface glycoproteins. Although the cysteine residues of B-type variant surface glycoproteins are located at completely different positions in the protein chain compared with A-type variant surface glycoproteins, the positions of the disulfide bonds can easily be integrated into the A-type tertiary structure. This result implies that, despite their enormous amino acid sequence variability, variant surface glycoproteins, regardless of their subtype, can fold into a similar tertiary structure.

IT 52-90-4, L-Cysteine, biological studies (detn. of disulfide bonds within a B domain variant surface glycoprotein from Trypanosoma congolense)

RN 52-90-4 HCA

CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

CC 6-3 (General Biochemistry)
 Section cross-reference(s): 10
ST variant surface glycoprotein BENat13 disulfide bond

location Trypanosoma

IT Glycolipoproteins

(VSG, BENat 1.3; detn. of disulfide bonds within a B domain variant surface glycoprotein from Trypanosoma congolense)

IT Disulfide group

Trypanosoma congolense

(detn. of disulfide bonds within a B domain variant surface glycoprotein from Trypanosoma congolense)

IT Tertiary structure

(protein; detn. of disulfide bonds within a B domain variant surface glycoprotein from Trypanosoma congolense)

- L98 ANSWER 22 OF 28 HCA COPYRIGHT 2004 ACS on STN

 123:50239 Production and Properties of Skeletal Myosin Subfragment 1
 Selectively Labeled with Fluorescein at Lysine-553 Proximal to the Strong Actin-Binding Site. Bertrand, Raoul; Derancourt, Jean;
 Kassab, Rhida (Centre de Recherches de Biochimie Macromoleculaire, Universite de Montpellier I, Montpellier, 34033, Fr.).

 Biochemistry, 34(29), 9500-7 (English) 1995. CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.
- AB We describe, for the first time, the reaction of skeletal myosin subfragment 1 (S-1) with the succinimido ester of 6-[fluorescein-5(and 6)-carboxamido]hexanoic acid (FHS), which takes place at pH 7.0, 20 .degree.C, within a 15 min period, in the presence of 1.5-1.8-fold molar excess of reagent over protein. As a result, 0.9-1.0 mol of fluorescyl group/mol of S-1 was covalently incorporated exclusively into the 95 kDa heavy chain as monitored by spectroscopic measurements. The central 50 kDa segment included the main site of fluorescence attachment as assessed by gel electrophoresis. The extent of S-1-FHS conjugation is strongly sensitive to F-actin binding but not to the interaction of nucleotides. The formation of the rigor F-actin-S-1 complex decreased the level of S-1 labeling to 20% without any competition between actin and S-1 for FHS binding. The derivatization of S-1did not alter the K+-ATPase activity, but it enhanced the Ca2+-ATPase and Mg2+-ATPase to 150% and 225%, resp., whereas it lowered the actin-activated ATPase to only 75% of the original activity. A double-reciprocal plot of the ATPase rate against actin concn. indicated a 2-fold decrease of the Vmax value for modified S-1, while the Km for actin was unchanged. Cosedimentation expts. did not reveal disruption of the rigor acto-S-1 interaction by the bound fluorophore. The labeled S-1 heavy chain was isolated, and its total tryptic digest was fractionated by reverse-phase HPLC. Only two fluorescent peptides, designated P-1 and P-2, contg.

15% and 85%, resp., of the initial fluorescence were found, and after purifn. they were entirely sequenced. The major P-2 peptide spanned the heavy chain sequence Ala-545-Lys-561 with Lys-553 identified as the FHS-hyperreactive residue; the sequence of the minor P-1 peptide corresponded to Gly-638-Lys-641 with Lys-640 being linked to FHS. The location of Lys-553 in the S-1 primary structure is of particular interest as it is relevant to the primary stereospecific and hydrophobic actin-binding site thought to involve the helix(Gly-516-Phe-542)-loop(Pro-543-Thr-546)-helix(Asp-547-His-558) motif residing in the lower subdomain of the 50 kDa region. Lys-553 is positioned at the end of the latter helix, and the fluorescyl group bound to it may represent a valuable landmark to probe the functioning and orientational properties of this strategic S-1 area during the acto-S-1-ATP interactions.

IT 148356-00-7 148356-01-8

(myosin subfragment 1 selectively labeled with fluorescein at lysine-553 proximal to the actin-binding site)

RN 148356-00-7 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-5-carboxamide, N-[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]-3',6'-dihydroxy-3-oxo-(9CI) (CA INDEX NAME)

RN 148356-01-8 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-6-carboxamide, N-[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]-3',6'-dihydroxy-3-oxo-(9CI) (CA INDEX NAME)

CC 6-3 (General Biochemistry)

IT 148356-00-7 148356-01-8

(myosin subfragment 1 selectively labeled with fluorescein at lysine-553 proximal to the actin-binding site)

L98 ANSWER 23 OF 28 HCA COPYRIGHT 2004 ACS on STN

122:234841 Specific binding assay compound with inhibitive self-quenching characteristics. Kline, Stanley (Enzo Diagnostics, Inc., USA). U.S. US 5384241 A 19950124, 6 pp. Cont. of U.S. Ser. No. 96,182, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1989-443812 19891129. PRIORITY: US 1987-96182 19870911.

Disclosed is an assay system including a compd. comprising an AΒ analyte-specific moiety having substituted thereon a polymer comprising plurality of self-quenching emitter moieties and a plurality of isocharged functionality sepg. the emitter moieties. The present invention provides compds. that overcome the undesirable effects of self-quenching when multiple emitter moieties are used for labeling of assay reagents. Avoidance of this self-quenching phenomenon by the compds. of the invention makes it possible to introduce a more concd. degree of labeling onto analyte-specific mols. such as oligonucleotide probes, antibodies and other specific binding proteins and analyte-specific polysaccharides. Therefore, it is possible to effect greater assay sensitivity because the no. of labels per recognition mol. (analyte-specific moiety) can be increased beyond the point previously possible without the redn. in signal caused by self-quenching.

IT 162224-11-5P

(specific binding assay compd. with inhibitive self-quenching characteristics)

RN 162224-11-5 HCA

CN Phosphoric acid, mono[2-[[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-6-yl)carbonyl]amino]ethyl] mono[2-[(2,5-dioxo-1-pyrrolidinyl)oxy]-2-oxoethyl] ester, polymer with aziridine (9CI) (CA INDEX NAME)

CM 1

CRN 162224-04-6

CMF C29 H23 N2 O14 P

CM 2

CRN 151-56-4

CMF C2 H5 N



IT 162224-04-6P

(specific binding assay compd. with inhibitive self-quenching characteristics)

RN 162224-04-6 HCA

CN Phosphoric acid, mono[2-[[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-6-yl)carbonyl]amino]ethyl]
mono[2-[(2,5-dioxo-1-pyrrolidinyl)oxy]-2-oxoethyl] ester (9CI) (CA INDEX NAME)

IC ICM C07H021-00

ICS G01N033-53; C12Q001-68

NCL 435006000

CC 9-5 (Biochemical Methods)

Section cross-reference(s): 3, 15

IT Dyes

Fluorescence quenching

Fluorescent substances

Isotope indicators

Nucleic acid hybridization

Phosphorescent substances

(specific binding assay compd. with inhibitive self-quenching characteristics)

IT Proteins, uses

(specific binding assay compd. with inhibitive self-quenching characteristics)

IT 9002-98-6DP, reaction with fluorescein derivs. 92557-81-8DP, conjugates with polymers and biopolymers 162224-03-5P

162224-11-5P 162224-12-6P

(specific binding assay compd. with inhibitive self-quenching characteristics)

IT 162224-04-6P

(specific binding assay compd. with inhibitive self-quenching characteristics)

- L98 ANSWER 24 OF 28 HCA COPYRIGHT 2004 ACS on STN
- 120:107724 Influence of the spectroscopic potential energy function SPASIBA on molecular dynamics of proteins: comparison with the AMBER potential. Derreumaux, Philippe; Vergoten, Gerard (INSERM U279 (SDI 15721), rue du Professeur Calmette, Lille, 59000, Fr.). THEOCHEM, 105(1-3), 55-64 (English) 1993. CODEN: THEODJ. ISSN: 0166-1280.
- The SPASIBA potential energy function developed for proteins on the AΒ basis of vibrational frequencies of peptides is compared to the AMBER force field by studying the mol. conformational flexibility of the alanine .alpha.-decapeptide and Ecballium elaterium trypsin inhibitor II (EETI-II), a 28-residues Two mol. dynamics (MD) simulations of 500ps duration using a distance-dependent dielec. function were carried out for the decapeptide with two different bond angle potential representations: the classical harmonic bond angle potential and the combination of this potential and the 1-3 geminal Urey-Bradley potential. The authors also performed two 200ps simulations of EETI-II with a sigmoidal distance-dependent function and examd. the effects of the V1-4tg energetics component, which deals with the 1-4 vicinal interactions taking effect on the dynamics in some side-chains. In comparing the MD results, the two potentials that better reproduce the obsd. vibrational frequencies act differently

on the flexibility of proteins. On the one hand, the Urey-Bradley potential increases the mobilities of backbone atoms; on the other hand, the V1-4tg potential generally constraints the side-chains to explore fewer conformations. Together, these results are in agreement with a better fit of the x-ray temp. factors, but do not give a new dynamic picture of proteins on a time scale less than lns, because localized rather than collective conformational changes are generated.

IT 52-90-4, Cysteine, properties 1632-99-1,

Hexadeuteroethane 1735-17-7, Cyclohexane-d12

(effect of potential energy functions on mol. dynamics calcns.)

RN 52-90-4 HCA

CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 1632-99-1 HCA

Ethane-d6 (6CI, 8CI, 9CI) (CA INDEX NAME)

CN

RN 1735-17-7 HCA

CN Cyclohexane-d12 (6CI, 8CI, 9CI) (CA INDEX NAME)

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 22

ST mol dynamics calcn peptide protein;

spectroscopic energy function mol dynamics

IT Peptides, properties

Proteins, properties

(effect of potential energy functions on conformations from mol. dynamics calcns.)

- IT Simulation and Modeling, physicochemical
 - (mol. dynamics, effect of potential energy functions on **peptide** and protein conformations from mol. dynamics calcns.)
- ΙΤ 52-90-4, Cysteine, properties 61-90-5, Leucine, properties 64-17-5, Ethanol, properties 72-19-5, Threonine, properties 74-82-8, Methane, properties 74-84-0, Ethane, properties 74-98-6, Propane, properties 75-08-1, Ethanethiol 78-78-4, 2-Methylbutane 75-28-5, Isobutane 79-05-0, Propionamide 79-16-3, N-Methylacetamide 110-82-7, Cyclohexane, properties 111-65-9, Octane, properties 124-18-5, Decane 463-82-1, Neopentane 624-89-5, Ethyl methyl sulfide 624-92-0, Dimethyl 1118-69-0, N-Isopropylacetamide 1632-99-1, Hexadeuteroethane 1735-17-7, Cyclohexane-d12 2675-88-9, N-Methylisobutyramide 7154-79-2, 2,2,3,3-Tetramethylpentane 13054-03-0, Glycyl-Lprolylalycylalycine
 - (effect of potential energy functions on mol. dynamics calcns.)
- L98 ANSWER 25 OF 28 HCA COPYRIGHT 2004 ACS on STN
- 114:203058 Affinity labeling of folate transport proteins with the N-hydroxysuccinimide ester of .gamma.-isomer of fluorescein-methotrexate. Fan, Jianguo; Pope, Laura E.; Vitols, Karin S.; Huennekens, F. M. (Res. Inst., Scripps Clin., La Jolla, CA, 92037, USA). Biochemistry, 30(18), 4573-80 (English) 1991. CODEN: BICHAW. ISSN: 0006-2960.
- AΒ Fluorescein-methotrexate, a deriv. in which the fluorophore is linked via a diaminopentane spacer to either the .alpha. - and .gamma.-carboxyl group of the glutamate moiety in the drug (Gapski et al., 1975), has been synthesized by an improved procedure and sepd. by DEAE-Trisacryl chromatog. into the .alpha.- and .gamma.-isomers (.alpha.-F-MTX and .gamma.-F-MTX). Each isomer was characterized by mass spectrometry, elemental anal., absorbance spectrum, TLC, and reversed-phase HPLC. Identity of the isomers was established by the following enzymic criteria: (a) .gamma.-F-MTX (but not the .alpha.-isomer) was hydrolyzed at the pteroate-glutamate bond by carboxypeptidase G2 to yield 4-amino-4-deoxy-10-methylpteroate and .gamma.-glutamyldiaminopentanefluorescein; and (b) .gamma.-F-MTX was a much better inhibitor of human dihydrofolate reductase than the .alpha.-isomer (Ki values of .alpha.- And .gamma.-F-MTX were comparable as 0.079 and 4.6 nM). inhibitors (Ki values of 1.6 and 0.6 .mu.M) of the transport system for reduced folates and MTX in L1210 cells, but the transporter in Lactobacillus casei was inhibited only by the .gamma.-isomer (Ki = 4.3 .mu.M). The .gamma.-isomer, therefore, was selected for

covalent labeling of proteins. When L. casei folate transport protein (18 kDa) was treated with .gamma.-F-MTX that had been activated with N-hydroxysuccinimide (NHS), the protein was readily visualized as a fluorescent band on SDS-PAGE electrophoretograms. The probe was also able to detect the transporter in membranes. SDS-PAGE anal. of a Triton X 100 ext. of L. casei membrane fragments that had been pretreated with activated .gamma.-F-MTX revealed only 2 fluorescent-labeled bands, viz., the 18-kDa transporter and an unidentified 33-kDa protein. The 43-kDa transporter for reduced foliate compds. and MTX in L1210 cells was also labeled by this procedure but, because of its relatively low level, visualization required immunopurifn., SDS-PAGE, and transfer to nitrocellulose, followed by immunoblotting with rabbit anti-fluorescein antibody/biotinylated goat anti-rabbit IgG/streptavidin-peroxidase conjugate. NHS-activated .gamma.-F-MTX also facilitated visualization, via fluorescence microscopy, of folate transporters on individual L1210 cells. The validity of this procedure was demonstrated by the marked redn. in fluorescence when labeling was conducted in the presence of excess MTX or when a mutant subline (R81) down-regulated for the transporter was used. L. casei spheroplasts treated with NHS-activated .gamma.-F-MTX were also fluorescent, and specificity was shown by reduced labeling in the presence of MTX. In this instance, however, the 33-kDa protein rather than the transporter appeared to be the labeled component.

IT 132884-74-3P

(prepn. of, for folate-transportin **protein** affinity labeling)

RN 132884-74-3 HCA

CN Pentanamide, 4-amino-N-[5-[[[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)amino]thioxomethyl]amino]pentyl]-5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-5-oxo-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

__ OH

CC 9-15 (Biochemical Methods)
Section cross-reference(s): 6

ST folate transport **protein** affinity labeling; fluorescein methotrexate ester **protein** affinity labeling

IT Lactobacillus casei

(folate-transporting **proteins** affinity labeling in, by fluorescein methotrexate hydroxysuccinimidyl ester)

IT Affinity

(labeling by, of folate-transporting proteins)

IT Microscopy

(fluorescence, of folate-transport proteins, fluorescein methotrexate hydroxysuccinimidyl ester in)

IT Proteins, specific or class

(folate-transporting, affinity labeling of, with fluorescein methotrexate hydroxysuccinimidyl ester)

IT 132884-72-1P

(prepn. of, folate-transporting protein affinity labeling in relation to)

IT 132884-74-3P

(prepn. of, for folate-transportin **protein** affinity labeling)

L98 ANSWER 26 OF 28 HCA COPYRIGHT 2004 ACS on STN
111:228613 Fluorescein-conjugated proteins with enhanced fluorescence. Ronald, Robert C.; Nguyen Phuc Huu; Rowley, Gerald L.

(Sclavo, Inc., USA). PCT Int. Appl. WO 8900291 A1 19890112, 30 pp. DESIGNATED STATES: W: AU, JP; RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1988-US2240 19880701. PRIORITY: US 1987-69288 19870701.

A method for detn. of an analyte, which comprises at least the step ABof binding a fluorescent-labeled reagent to the analyte, uses a fluorescent-labeled reagent which is a ligand labeled with a substituent FlNHCZCR2 (I; Fl = fluorescein; Z = O, S; R = H, C1-4 alkyl). Fluorescein I (5-Fl-NHCOCH2S(CH2)2COOEt) (II) was prepd. from the reaction of 3-mercaptopropionic acid (80 .mu.L in 6 mL DMF and 3 mL 50 mM phosphate, 2.5 mM EDTA buffer, pH 6.30) with 5-iodoacetamidofluorescein (200 mg in 7 mL DMF and 4 mL of the same buffer) in Tris buffer overnight at 50.degree.. II 1.28 was reacted with N-hydroxysuccinimide 3.45 and 1-(3-dimethylaminopropyl)-3ethylcarbodiimide 4.22 mg in anhyd. DMF for 7 h at room temp. resultant N-hydroxysuccinimide ester was conjugated to rabbit IgG Fab' fragments, which were then conjugated to .alpha .fetoprotein through a sulfosuccinimidyl linker. Patient serum samples, the labeled .alpha.-fetoprotein reagent, buffer, and goat anti-.alpha.-fetoprotein antibody were mixed and incubated for 2.5 h at 37.degree.. Rabbit antigoat Ig antibody was added, followed by PEG and incubation for 30 min at room temp. The ppt. was dissolved in measurement buffer and fluorescence was measured. .alpha.-Fetoprotein was detd. by comparison to a std. curve.

IT 123761-26-2P 123761-28-4P

(prepn. of, as fluorescent label)

RN 123761-26-2 HCA

CN Acetamide, N-(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)-2-[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropyl]thio]- (9CI) (CA INDEX NAME)

N— O— C—
$$CH_2$$
— CH_2 — S — CH_2 — C — NH — O

RN 123761-28-4 HCA

CN Acetamide, N-(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)-2-[[2-[(2,5-dioxo-1-pyrrolidinyl)oxy]-2-

oxoethyl]dithio]- (9CI) (CA INDEX NAME)

RN 123761-26-2 HCA

CN Acetamide, N-(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)-2-[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropyl]thio]- (9CI) (CA INDEX NAME)

N— O— C—
$$CH_2$$
— CH_2 — S — CH_2 — C — NH — O

IC ICM G01N033-53

ICS G01N033-533; C07D311-82

CC 9-14 (Biochemical Methods)

Section cross-reference(s): 28, 79, 80

ST fluorescein amido deriv protein label; fetoprotein fluorescein label immunoassay

IT Ligands

Proteins, uses and miscellaneous

(fluorescein-labeled, for fluorescence anal.)

IT Blood analysis

(.alpha.-fetoprotein immunochem. detn. in human, fluorescein deriv.-labeled .alpha.-fetoprotein in)

IT Fetoproteins

(.alpha.-, conjugates, with fluorescein deriv.-labeled IgG Fab', prepn. of, for .alpha.-fetoprotein immunochem. detn. in serum)

IT 120858-32-4P 123740-08-9P **123761-26-2P** 123761-27-3P **123761-28-4P**

(prepn. of, as fluorescent label)

IT 123761-26-2DP, IgG reaction products, .alpha.fetoprotein conjugates

(prepn. of, as fluorescent tracer)

- IT 103708-09-4DP, .alpha.-fetoprotein reaction products (prepn. of, in prepn. of fluorescent tracer)
- L98 ANSWER 27 OF 28 HCA COPYRIGHT 2004 ACS on STN 109:69743 Rapid analysis of proteins and peptides by reversed-phase chromatography and polymeric micropellicular sorbents. Maa, Yih Fen; Horvath, Csaba (Dep. Chem. Eng., Yale Univ., New Haven, CT, 06520, USA). Journal of Chromatography, 445(1), 71-86 (English) 1988. CODEN: JOCRAM. ISSN: 0021-9673.
- Peptides and proteins were sepd. by reversed-phase chromatog. on a AB 30 .times. 4.6 mm I.D. column packed with nonporous crosslinked polystyrene particles having a mean particle diam. of 3 .mu.m and a rugulose surface. The polymeric support did swell slightly in org. solvents, but the estd. 5-8% change in particle diam. did not adversely affect the efficiency of the column which was used repeatedly with gradient elution from water to org. solvent under conditions typically employed in reversed-phase chromatog. these expts., the pH of the eluent was varied in a wide range to compare the effect of acidic and alk. eluents on the sepn. of protein and complex peptide mixts. The column showed no deterioration even after extensive exposure to alk. mobile phases. The retention behavior of 16 proteins having widely different pI values was studied as a function of the eluent pH. The chromatog. system exhibited large selectivity differences upon changing the pH of the eluent from 2 to 11. Anal. information about peptide and protein mixts. could therefore be enhanced by using eluents at the pH extremes. At the pH extremes of 2 and 11 peak sharpness and protein mass recovery were superior to those obtained with neutral eluents. Usually the column temp. was held at 80.degree. and typical anal. times ranged from 30 s to 10 min as illustrated by chromatograms of protein mixts. and by peptide maps. With regular use under such conditions, the column showed no deterioration after 3 mo.
- IT 599-00-8

(in proteins reversed-phase HPLC) RN 599-00-8 HCA Acetic acid-d, trifluoro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME) CN D-0-C-CF3 9-3 (Biochemical Methods) CC ITAgglutinins and Lectins Albumins, analysis Conalbumins Fetuins Hemoglobins Myoglobins Ovalbumins Peptides, analysis Proteins, analysis Transferrins (chromatog. of, reversed-phase high-performance liq., on polymeric micropellicular sorbent) ΙT 9003-70-7, **Styrene**-divinylbenzene copolymer (as stationary phase, in reversed-phase HPLC of peptides and protein) ΙΤ 599-00-8 (in proteins reversed-phase HPLC) L98 ANSWER 28 OF 28 HCA COPYRIGHT 2004 ACS on STN 107:52516 Isolation of products and intermediates of pancreatic prosomatostatin processing: use of fast atom bombardment mass spectrometry as an aid in analysis of prohormone processing. Andrews, P. C.; Dixon, Jack E. (Dep. Biochem., Purdue Univ., West Lafayette, IN, 47907, USA). Biochemistry, 26(15), 4853-61 (English) 1987. CODEN: BICHAW. 0006-2960. Major products and an intermediate in the proteolytic processing AB pathway of preprosomatostatin I from anglerfish (Lophius americanus) were purified and characterized. Proteolytic mapping by fast atom bombardment mass spectrometry was used to rapidly locate regions of the peptides whose masses deviated from those deduced from the cDNA sequence. Amino acid anal. and partial Edman sequencing were also used to confirm the structure. The protein structural data indicate a glutamate for glycine substitution at position 83 of preprosomatostain I (aPPSS-I, numbering from the initiator methonine) relative to the cDNA sequence. Two of the

peptides isolated, aPPSS-I (26-52) (7.5 nmol/g), and aPPSS-I

(26-92) (49.5 nmol/g), define signal cleavage as occurring between cysteine and serine at positions 25 and 26, resp. A partial sequence was obtained from fragment ions in the mass spectrum of a peptide corresponding to aPPSS-I (94-105) (58 nmol/g). The 14-residue somatostatin [SS-14 corresponding to aPPSS-I (108-121)] was isolated previously. Taken together, these peptides suggest a pathway for prosomatostatin I processing in which the residues corresponding to ss-14 and the immediately preceding 14 residues are cleaved from the prohormone via endoproteolysis (order of cleavage not detd.). The fragment aPPSS-I (94-105) was isolated in lower yield than ss-14 and may represent a secondary site of cleavage. Subsequent cleavage at arginine-53 results in the minor peptide aPPSS-I (26-52). The terminal basic amino acids generated by endoproteolytic processing were not found for any of the peptides isolated. The peptides described were identified as products of aPPSS-I processing in radiolabeling studies with intact anglerfish islets. 2-6 (Mammalian Hormones) Section cross-reference(s): 12

=> d 199 1-28 cbib abs hitstr hitind

CC

ANSWER 1 OF 28 HCA COPYRIGHT 2004 ACS on STN 139:113655 Fluorescent serine protease affinity labeling agents and methods for determining apoptotic state of cells. Phelps, David J.; Johnson, Gary L.; Lee, Brian W.; Darzynkiewicz, Zbigniew; Grabarek, Jerzy (Immunochemistry Technologies, LLC, USA). PCT Int. Appl. WO 2003059877 A2 20030724, 53 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US40920 20021219. PRIORITY: US 2001-PV342955 20011221.

The invention provides novel serine protease affinity labels L-A-X-NHCH(R')C(:O)CH2Cl (L = label; A = bond or linker; X = absent, amino acid, peptide; R' = H, (substituted)Cl-6-alkyl) or salts thereof, as well as compns. comprising such compds. or salts. The compn. of the amino acid side-chain (R') along with the amino acid or amino acid sequence (peptide) of the X component of the affinity label affect the target selectivity of the labeled affinity ligand. Utilization of cell-permeable, enzyme-selective,

labeled affinity ligands provides a precise mechanism for evaluating the current and future status of cell populations. Thus, the induction of **proteinases** in camptothecin-treated HL-60 cells was obsd. by fluorescence microscopy after addn. of serine **proteinase** affinity inhibitors 5(6)-carboxyfluoresceinyl-L-phenylalanylchloromethyl ketone (FFCK) and 5(6)-carboxyfluoresceinyl-L-leucylchloromethyl ketone (FLCK) and caspase affinity inhibitor 5(6)-carboxyfluoresceinyl-L-valylalanylaspartylfluoromethyl ketone (FAM-VAD-FMK).

IT 474255-88-4

(FFCK; fluorescent serine protease affinity labeling agents and methods for detg. apoptotic state of cells)

RN 474255-88-4 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-ar-carboxamide, N-[(1S)-3-chloro-2-oxo-1-(phenylmethyl)propyl]-3',6'-dihydroxy-(9CI) (CA INDEX NAME)

IT 560094-67-9

(FKCK; fluorescent serine protease affinity labeling agents and methods for detg. apoptotic state of cells)

RN 560094-67-9 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-ar-carboxamide, N-[(1S)-5-amino-1-(chloroacetyl)pentyl]-3',6'-dihydroxy-3-oxo- (9CI) (CA INDEX NAME)

IT 475570-57-1

(FLCK; fluorescent serine protease affinity labeling agents and methods for detg. apoptotic state of cells)

RN 475570-57-1 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-ar-carboxamide,
N-[(1S)-1-(chloroacetyl)-3-methylbutyl]-3',6'-dihydroxy-3-oxo- (9CI)
(CA INDEX NAME)

IT 560094-68-0

RN 560094-68-0 HCA

43

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-ar-carboxamide, N-[(1S)-4-[(aminoiminomethyl)amino]-1-(chloroacetyl)butyl]-3',6'-dihydroxy-3-oxo-(9CI) (CA INDEX NAME)

IC ICM CO7D

CC 7-1 (Enzymes)

Section cross-reference(s): 1

ST apoptosis serine **proteinase** fluorescent affinity label; disease cancer **diagnosis** serine **proteinase** fluorescent affinity label

IT 474255-88-4

(FFCK; fluorescent serine protease affinity labeling agents and methods for detg. apoptotic state of cells)

IT 560094-67-9

(FKCK; fluorescent serine protease affinity labeling agents and methods for detg. apoptotic state of cells)

IT 475570-57-1

(FLCK; fluorescent serine protease affinity labeling agents and methods for detg. apoptotic state of cells)

IT 560094-68-0

(FRCK; fluorescent serine protease affinity labeling agents and methods for detg. apoptotic state of cells)

IT 37259-58-8, Serine **proteinase** 186322-81-6, Caspase (fluorescent serine protease affinity labeling agents and methods for detg. apoptotic state of cells)

L99 ANSWER 2 OF 28 HCA COPYRIGHT 2004 ACS on STN 138:397832 NMR Structure of a Rifunctional Rhodamir

138:397832 NMR Structure of a Bifunctional Rhodamine Labeled N-Domain of Troponin C Complexed with the Regulatory "Switch" Peptide from Troponin I: Implications for in Situ Fluorescence Studies in Muscle Fibers. Mercier, Pascal; Ferguson, Roisean E.; Irving, Malcolm; Corrie, John E. T.; Trentham, David R.; Sykes, Brian D. (CIHR Group in Protein Structure and Function, Department of Biochemistry, University of Alberta, Edmonton, AB, T6G 2H7, Can.). Biochemistry, 42(15), 4333-4348 (English) 2003. CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.

AB The structure of the calcium-satd. regulatory domain of skeletal troponin C (sNTnC) complexed with the switch peptide comprising residues 115-131 of troponin I (TnI), and with a bifunctional rhodamine fluorescent label attached to residues 56 (E56C) and 63 (E63C) on the C helix of sNTnC, has been detd. using NMR spectroscopy. The structure shows that the integrity of the C helix is not altered by the E(56,63)C mutations or by the presence of the bifunctional rhodamine and that the label does not interact with the hydrophobic cleft of sNTnC. Moreover, the overall fold of the protein and the position of the TnI peptide are similar to those obsd. previously with related cardiac NTnC complexes with residues 147-163 of cardiac TnI [Li et al. (1999) Biochem. 38, 8289-8298] and including the drug bepridil [Wang et al. (2002) J. Biol. Chem. 277, 31124-31133]. The degree of opening of the structure is reduced as compared to that of calcium-satd. sNTnC in the absence of the switch peptide [Gagne et al. (1995) Nat. Struct. Biol. 2, 784-789]. The switch peptide is bound in a shallow and complementary hydrophobic surface cleft largely defined by helixes A and B and also has key ionic interactions with sNTnC. These results show that bifunctional rhodamine probes can be attached to surface helixes via suitable pairs of solvent-accessible residues that have been mutated to

IT 203580-70-5

, ò

(bifunctional rhodamine probes can be used to det. orientation and motion of regulatory domain of troponin C-switch **peptide** from troponin I complex without altering conformation of labeled domain)

RN 203580-70-5 HCA

11(4), in press].

CN Acetamide, N,N'-[(3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthene]-3',6'-diyl)bis[(methylimino)-2,1-ethanediyl]]bis[2-iodo-(9CI) (CA INDEX NAME)

cysteines, without altering the conformation of the labeled

domain. A set of such probes can be used to det. the orientation and motion of the target domain in the cellular environment [Corrie et al. (1999) Nature 400, 425-430; Ferguson et al. (2003) Mol. Cell

CC 6-3 (General Biochemistry)

ST rhodamine troponin complex **peptide** muscle fiber conformation electrostatic force

IT Troponins

į Š

(C; bifunctional rhodamine probes can be used to det. orientation and motion of regulatory domain of troponin C-switch peptide from troponin I complex without altering conformation of labeled domain)

IT Troponins

(I, switch peptide of troponin C; bifunctional rhodamine probes can be used to det. orientation and motion of regulatory domain of troponin C-switch peptide from troponin I complex without altering conformation of labeled domain)

IT Electrostatic force

Molecular association

(bifunctional rhodamine probes can be used to det. orientation and motion of regulatory domain of troponin C-switch peptide from troponin I complex without altering conformation of labeled domain)

IT Muscle

(fiber; bifunctional rhodamine probes can be used to det. orientation and motion of regulatory domain of troponin C-switch peptide from troponin I complex without altering conformation of labeled domain)

IT Protein motifs

(regulatory; bifunctional rhodamine probes can be used to det. orientation and motion of regulatory domain of troponin C-switch **peptide** from troponin I complex without altering conformation of labeled domain)

IT Self-association

(troponin C in complex with switch **peptide** of troponin I shows dimerization)

IT 203580-70-5

(bifunctional rhodamine probes can be used to det. orientation and motion of regulatory domain of troponin C-switch **peptide** from troponin I complex without altering conformation of labeled domain)

- L99 ANSWER 3 OF 28 HCA COPYRIGHT 2004 ACS on STN
 138:395285 An improved method of evaluation of drug-evoked changes in gastric emptying in mice. Osinski, M. A.; Seifert, T. R.; Cox, B. F.; Gintant, G. A. (Department of Integrative Pharmacology, Abbott Laboratories, Abbott Park, IL, 60064-6119, USA). Journal of Pharmacological and Toxicological Methods, 47(2), 115-120 (English) 2002. CODEN: JPTMEZ. ISSN: 1056-8719. Publisher: Elsevier Science Inc..
- The increased availability of transgenic mice prompts a need for the AB adaptation to mice of whole-animal assays traditionally performed in larger lab. animals. Gastric emptying studies are frequently conducted in dogs and rats. Mouse-based gastric emptying models currently available often use inert, nonnutrient liq. meals contg. nonabsorbable markers or radionuclides. We have developed a mouse gastric emptying assay that features a favorable throughput and the use of a semisolid, high-calorie meal. carbohydrate- and protein-rich semisolid test meal was prepd. from common lab. reagents. Gastric emptying was detd. by subtracting the mass of test meal remaining in the stomach from the mass of test meal administered. A time-course study of basal emptying of a semisolid, paste-like test meal high in carbohydrate and protein from the stomachs of overnight-fasted mice was conducted. Agents known to either inhibit (propantheline, 0.3-10 mg/kg s.c.; corticotropin-releasing factor [CRF], 3-100 nmol/kg i.p.) or accelerate (metoclopramide, 1-10 mg/kg i.p.; bethanechol, 1-30 mg/kg i.p.) gastric emptying were tested. single time-point variation of the assay can be used for quickly screening compds. for effects on gastric emptying. In time-course studies, the test meal emptied from the stomach with a half-emptying time of 30.6 min (95% CI: 27.3-34.7). The gastric emptying data were successfully modeled by a two-parameter exponential decay No lag phase was obsd., indicating that the meal empties from the stomach as a liq. The anticholinergic agent propantheline

increased gastric half-emptying time (t1/2) approx. threefold, while metoclopramide decreased gastric half-emptying time approx. twofold compared to basal emptying. Single time-point screening studies correctly detected the gastrokinetic activity of bethanechol and the inhibitory effect of CRF. The mouse gastric emptying assay reported here is simple, inexpensive, and not labor-intensive. It is capable of detecting either stimulation or inhibition of gastric motor This assay should prove useful for identifying drug-evoked changes in gastric emptying as well as for assessing the gastric motility effects of altered gene expression in genetically modified mice.

IT 50-34-0, Propantheline bromide (method for evaluation of drug-evoked changes in mice gastric emptying) RN

50-34-0 HCA

2-Propanaminium, N-methyl-N-(1-methylethyl)-N-[2-[(9H-xanthen-9- $^{\circ}$)-N-[2-[(9H-xanthen-9- $^{\circ}$)-[2-[(9H-xanthen-9- $^{\circ}$)-[2-[(9H-xanthen-9-])-[2-[(9H-xanthen-9-])-[2-[(9H-xanthen-9-])-CN ylcarbonyl)oxy]ethyl]-, bromide (9CI) (CA INDEX NAME)

Br-

1-1 (Pharmacology) CC ΙT

50-34-0, Propantheline bromide 674-38-4, Bethanechol 7232-21-5, Metoclopramide hydrochloride (method for evaluation of drug-evoked changes in mice gastric emptying)

ANSWER 4 OF 28 HCA COPYRIGHT 2004 ACS on STN

138:390922 Arsenide compound system for selective targeting of apoptotic cells. Hogg, Philip John (Unisearch Limited, Australia). PCT Int. Appl. WO 2003039564 A1 20030515, 85 pp. DESIGNATED STATES: W: AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE,

BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-AU1523 20021108. PRIORITY: AU 2001-8746 20011108.

The invention discloses a method of selectively targeting an active agent (or agent capable of becoming an active agent) to apoptotic cells in a vertebrate, comprising administering to the vertebrate a system comprising an arsenoxide (or arsenoxide equiv.) compd. and the agent, wherein the system selectively targets apoptotic cells. Prepn. of e.g. 4-[N-(S-glutathionylacetyl)amino]phenylarsenoxide is described.

IT 123761-26-2

(arsenide compd. system for selective targeting of apoptotic cell)

RN 123761-26-2 HCA

CN Acetamide, N-(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)-2-[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropyl]thio]-(9CI) (CA INDEX NAME)

IC ICM A61K033-36

ICS A61K047-04; A61P035-00; A61P019-00; A61P009-10

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 8, 9, 29

IT Proteins

(RIP (ribosome-inactivating **protein**); arsenide compd. system for selective targeting of apoptotic cell)

IT Amines, biological studies

Amino acids, biological studies

Oligosaccharides, biological studies

Peptides, biological studies

Proteins

(conjugates; arsenide compd. system for selective targeting of apoptotic cell)

IT 37318-49-3, **Protein disulfide** isomerase (arsenide compd. system for selective targeting of apoptotic

cell) 98-50-0, p-Arsanilic acid 70-18-8, Glutathione, reactions ΙΤ 598-21-0, Bromoacetyl bromide 89889-52-1 **123761-26-2** (arsenide compd. system for selective targeting of apoptotic cell) ANSWER 5 OF 28 HCA COPYRIGHT 2004 ACS on STN 137:381966 Methods and compositions for analyzing Singh, Sharat; Salimi-Moosavi, Hossein; Tahir, proteins. Syed Hasan; Wallweber, Gerald J.; Kirakossian, Hrair; Matray, Tracy J.; Hernandez, Vincent S. (Aclara Biosciences, Inc., USA). PCT Int. Appl. WO 2002095356 A2 20021128, 141 pp. DESIGNATED STATES: W: AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US16098 20020521. PRIORITY: US 2001-PV292548 20010521; US 2001-PV334901 20011024. The invention concerns methods, compns. and kits are disclosed for AB detg. one or more target polypeptides in a sample where the target polypeptides have undergone a post-translational modification. A mixt. comprising the sample and a first reagent comprising a cleavage-inducing moiety and a first binding agent for a binding site on a target polypeptide is subjected to conditions under which binding of resp. binding moieties occurs. The binding site is the result of post-translational modification activity involving the target polypeptide. The method may be employed to det. the target polypeptide itself. In another embodiment the presence and/or amt. of the target polypeptide is related to the presence and/or amt. and/or activity of an agent such as an enzyme involved in the post-translational modification of the target polypeptide. The interaction between the first binding agent and the binding site brings the cleavage-inducing moiety into close proximity to a cleavable moiety, which is assocd. with the polypeptide and is susceptible to cleavage only when in proximity to the cleavage-inducing moiety. In this way, an electrophoretic tag for each of the polypeptides may be released. Released electrophoretic tags are sepd. and the presence and/or amt. of the target polypeptides are detd. based on the corresponding electrophoretic tags. 331834-87-8P 476348-24-0P 476348-27-3P

476348-30-8P 476348-33-1P 476348-36-4P 476348-39-7P 476348-40-0P 476348-43-3P

TT

476348-46-6P 476348-52-4P 476349-15-2P 476360-19-7P 476360-20-0P 476360-21-1P 476360-22-2P

(methods and compns. for analyzing proteins)

331834-87-8 HCA RN

CN

Acetamide, N-(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H] xanthen] -6-yl)-2-[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3oxopropyl]thio]- (9CI) (CA INDEX NAME)

476348-24-0 HCA RN CN

Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-5-carboxamide, N-[3-[[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3oxopropyl]thio]acetyl]amino]-2,2-dimethylpropyl]-3',6'-dihydroxy-3-OXO- (9CI) (CA INDEX NAME)

> PAGE 1-A HO__

RN 476348-27-3 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-5-carboxamide,
N-[2-[[[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3oxopropyl]thio]acetyl]amino]ethyl]-3',6'-dihydroxy-3-oxo- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 476348-30-8 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-5-carboxamide,
N-[10-[[[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3oxopropyl]thio]acetyl]amino]decyl]-3',6'-dihydroxy-3-oxo- (9CI) (CA
INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 476348-33-1 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-5-carboxamide, N-[15-[(2,5-dioxo-1-pyrrolidinyl)oxy]-10,15-dioxo-3,6-dioxa-12-thia-9-azapentadec-1-yl]-3',6'-dihydroxy-3-oxo-(9CI) (CA INDEX NAME)

PAGE 1-B

RN 476348-36-4 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-5-carboxamide,
N-[20-[(2,5-dioxo-1-pyrrolidinyl)oxy]-15,20-dioxo-4,7,10-trioxa-17thia-14-azaeicos-1-yl]-3',6'-dihydroxy-3-oxo- (9CI) (CA INDEX NAME)

PAGE 1-B

RN 476348-39-7 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-5-carboxamide,
N-[[4-[[[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3oxopropyl]thio]acetyl]amino]methyl]phenyl]methyl]-3',6'-dihydroxy-3oxo- (9CI) (CA INDEX NAME)

PAGE 1-B

RN 476348-40-0 HCA

CN

Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-6-carboxamide, N-[3-[[[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3oxopropyl]thio]acetyl]amino]-2,2-dimethylpropyl]-3',6'-dihydroxy-3oxo- (9CI) (CA INDEX NAME)

HO_

PAGE 1-B

RN 476348-43-3 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-6-carboxamide, N-[2-[[[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3oxopropyl]thio]acetyl]amino]ethyl]-3',6'-dihydroxy-3-oxo- (9CI) (CA INDEX NAME)

PAGE 1-A

HO__

·	

RN 476348-46-6 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-6-carboxamide,
N-[15-[(2,5-dioxo-1-pyrrolidinyl)oxy]-10,15-dioxo-3,6-dioxa-12-thia9-azapentadec-1-y1]-3',6'-dihydroxy-3-oxo-(9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

RN 476348-52-4 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-6-carboxamide, N-[20-[(2,5-dioxo-1-pyrrolidinyl)oxy]-15,20-dioxo-4,7,10-trioxa-17-thia-14-azaeicos-1-yl]-3',6'-dihydroxy-3-oxo-(9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

٤

RN 476349-15-2 HCA CN Acetamide, N-[2-[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)amino]-2-oxoethyl]-2-[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropyl]thio]- (9CI) (CA INDEX NAME)

__ OH

RN 476360-19-7 HCA
CN Butanoic acid, 4-[[3-[[(3',6'-dihydroxy-3-oxospiro[isobenzofuran1(3H),9'-[9H]xanthen]-6-yl)carbonyl]amino]-2,2-dimethylpropyl]amino]3-[[[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3oxopropyl]thio]acetyl]amino]-4-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 476360-20-0 HCA

CN L-.alpha.-Asparagine, N-[[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropyl]thio]acetyl]-L-.alpha.-aspartyl-N-[2-[[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)carbonyl]amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

RN 476360-21-1 HCA
CN Phosphonic acid, [2-[[2-[[(3',6'-dihydroxy-3-oxospiro[isobenzofuran1(3H),9'-[9H]xanthen]-5-yl)carbonyl]amino]ethyl]amino]-1-[[[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropyl]thio]acetyl]amino]-2-oxoethyl](9CI) (CA INDEX NAME)

PAGE 1-A

RN 476360-22-2 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-5-carboxamide,
N-[2-[[[[11-[(2,5-dioxo-1-pyrrolidinyl)oxy]-11oxoundecyl]thio]phenylacetyl]amino]ethyl]-3',6'-dihydroxy-3-oxo(9CI) (CA INDEX NAME)

PAGE 1-A

IT 123761-26-2P

(methods and compns. for analyzing proteins)

RN 123761-26-2 HCA

CN Acetamide, N-(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)-2-[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropyl]thio]- (9CI) (CA INDEX NAME)

N— O— C—
$$CH_2$$
— CH_2 — S — CH_2 — C — NH — O

IC ICM GO1N

CC 9-16 (Biochemical Methods)

Section cross-reference(s): 6

ST phosphorylation **protein** chromatog reagent tags photosensitizer antibody immunoassay

IT Immunoglobulins

(G; methods and compns. for analyzing proteins

IT Antibodies

(as electrophoretic probes, conjugated with e-tags; methods and compns. for analyzing proteins)

IT Spheres

(beads, photosensitizer; methods and compns. for analyzing proteins)

```
ΙT
     Glycosylation
        (biol.; methods and compns. for analyzing
        proteins)
     Enzymes, uses
ΙΤ
        (cofactors; methods and compns. for analyzing
        proteins)
ΙT
     Ligands
        (for protein receptors; methods and compns. for
        analyzing proteins)
     Affinity chromatography
ΙT
        (immobilized metal (IMAC); methods and compns. for
        analyzing proteins)
     Lipids, uses
IT
        (lipidation; methods and compns. for analyzing
        proteins)
IT
     Acetylation
     Acylation
     Bond cleavage
     Electrophoresis
     Hydrolysis
     Immunoassay
     Isoprenylation
     Methylation
     Phosphate group
     Phosphorylation, biological
     Photosensitizers (pharmaceutical)
     Ribosylation
     Test kits
        (methods and compns. for analyzing proteins)
ΙΤ
     Cytokines
       Peptides, analysis
        (methods and compns. for analyzing proteins)
     Agglutinins and Lectins
ΙT
         (methods and compns. for analyzing proteins)
IT
     Porphyrins
        (methods and compns. for analyzing proteins)
ΙT
         (methods and compns. for analyzing proteins)
ΙΤ
     Alkenes, properties
     Thioethers
         (methods and compns. for analyzing proteins)
IT
     Receptors
         (protein; methods and compns. for analyzing
        proteins)
ΙT
     Ethers, properties
         (seleno-; methods and compns. for analyzing
        proteins)
ΙΤ
     Enzymes, uses
```

```
(substrates; methods and compns. for analyzing
       proteins)
ΙT
    Enzymes, uses
        (subunits; methods and compns. for analyzing
                     13780-71-7, Boronic acid
ΤT
     58-85-5, Biotin
        (contg.-moieties; methods and compns. for analyzing
       proteins)
     150347-54-9
TT
        (methods and compns. for analyzing proteins)
    331834-87-8P 476348-24-0P 476348-27-3P
ΙΤ
     476348-30-8P 476348-33-1P 476348-36-4P
     476348-39-7P 476348-40-0P 476348-43-3P
     476348-46-6P 476348-52-4P
                              476349-14-1P
     476349-15-2P 476360-19-7P 476360-20-0P
     476360-21-1P 476360-22-2P
        (methods and compns. for analyzing proteins)
     574-93-6, Phthalocyanine 2122-46-5, Phenoxy radical 3352-57-6,
ΙΤ
                                  7722-84-1, Hydrogen peroxide,
    Hydroxy radical, properties
                 11062-77-4, Superoxide anion
    properties
        (methods and compns. for analyzing proteins)
                                    2321-07-5D, Fluorescein, halogenated
     81-88-9D, halogenated derivs.
ΙΤ
              23627-89-6, Naphthalocyanine
        (methods and compns. for analyzing proteins)
     288-32-4, Imidazole, properties 288-42-6, Oxazole 288-47-1,
IT
     Thiazole
        (methods and compns. for analyzing proteins)
                                               106755-09-3P
                                106754-85-2P
ΙΤ
     63368-54-7P
                  73264-12-7P
                  136091-82-2P
                                  148942-72-7P
                                                 476348-55-7P
     123761-26-2P
                                                 476348-69-3P
                  476348-62-6P
                                  476348-65-9P
     476348-59-1P
     476348-72-8P 476348-77-3P 476348-80-8P
                                                 476348-83-1P
                                  476348-92-2P
                                                 476348-94-4P
     476348-86-4P 476348-89-7P
     476348-96-6P 476348-99-9P
                                                 476349-05-0P
                                  476349-02-7P
     476349-08-3P
                   476349-24-3P
                                  476349-28-7P
        (methods and compns. for analyzing proteins)
     7782-44-7, Oxygen, properties
ΙT
        (singlet; methods and compns. for analyzing
        proteins)
ΙΤ
     60267-61-0, Ubiquitin
        (ubiquitination; methods and compns. for analyzing
        proteins)
    ANSWER 6 OF 28 HCA COPYRIGHT 2004 ACS on STN ~
L99
137:257647 Use of a substantially cell membrane impermeable arsenoxide
     compound for treating arthritis. Hogg, Philip John; Donoghue, Neil
     (Unisearch Limited, Australia). PCT Int. Appl. WO 2002074305 A1
     20020926, 91 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ,
```

BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ,

EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-AU310 20020319. PRIORITY: AU 2001-3798 20010319.

The invention provides a method of treatment and/or prophylaxis of arthritis in a vertebrate, comprising administering a therapeutically effective amt. of a compd. A-(L-Y)p [A = at least one substantially cell-membrane impermeable pendant group; L = linker and/or spacer group; Y = at least one arsenoxide or arsenoxide equiv.; p = 1-10; the sum total of carbon atoms in A and L together is greater than 6], or a pharmaceutically acceptable salt thereof, optionally together with a pharmaceutically acceptable carrier, diluent or excipient. Prepn. of compds. of the invention is described.

IT 52-90-4D, L-Cysteine, derivs.

(cell membrane impermeable arsenoxide compd. for treating arthritis)

RN 52-90-4 HCA

CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 123761-26-2 148356-00-7 148356-01-8

(reaction; cell membrane impermeable arsenoxide compd. for treating arthritis)

RN 123761-26-2 HCA

CN Acetamide, N-(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)-2-[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropyl]thio]- (9CI) (CA INDEX NAME)

RN 148356-00-7 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-5-carboxamide, N-[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]-3',6'-dihydroxy-3-oxo-(9CI) (CA INDEX NAME)

RN 148356-01-8 HCA

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-6-carboxamide, N-[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]-3',6'-dihydroxy-3-oxo- (9CI) (CA INDEX NAME)

```
ΙC
     ICM A61K031-285
     ICS A61P019-02
CC
     1-7 (Pharmacology)
     Section cross-reference(s): 34, 63
ΙT
     Proteins
        (endothelial cell surface; cell membrane impermeable arsenoxide
        compd. for treating arthritis)
ΙΤ
    Amines, biological studies
     Amino acids, biological studies
     Oligosaccharides, biological studies
       Peptides, biological studies
      Proteins
        (linked arsenoxide derivs.; cell membrane impermeable arsenoxide
        compd. for treating arthritis)
ΙT
     Sulfhydryl group
        (proteins contq., linked arsenoxide derivs.; cell
       membrane impermeable arsenoxide compd. for treating arthritis)
ΙΤ
     59-52-9, 2,3,-Dimercapto-1-propanol
                                         1077-28-7, 6,8-Thioctic acid
     3483-12-3, Dithiothreitol 37318-49-3, Protein
                          117525-19-6
    disulfide isomerase
                                        331722-91-9
        (cell membrane impermeable arsenoxide compd. for treating
        arthritis)
ΙT
    52-90-4D, L-Cysteine, derivs.
                                    56-84-8D,
    L-Aspartic acid, linked arsenoxide derivs.
                                                56-86-0D, L-Glutamic
    acid, linked arsenoxide derivs. 56-87-1D, L-Lysine, linked
                         58-85-5D, Biotin, linked arsenoxide derivs.
    arsenoxide derivs.
                                    70-18-8D, Glutathione, linked
    70-18-8D, Glutathione, derivs.
    arsenoxide derivs. 74-79-3D, L-Arginine, linked arsenoxide derivs.
     498-40-8D, Cysteic acid, linked arsenoxide derivs.
                                                        2321-07-5D,
     Fluorescein, linked arsenoxide derivs. 3416-24-8D, Glucosamine,
                                19246-18-5D, derivs.
    linked arsenoxide derivs.
                                                       19246-18-5D,
    Cysteinylglycine, linked arsenoxide derivs.
                                                  172777-84-3D, Cy 5.5,
    linked arsenoxide derivs. 331815-00-0 331815-01-1
                                                            331815-02-2
     331815-03-3 331815-04-4 331815-05-5 331815-06-6
                                                            331815-07-7
     331815-08-8
                  331815-09-9 331815-10-2 463313-69-1 463313-70-4
     463313-71-5
        (cell membrane impermeable arsenoxide compd. for treating
       arthritis)
ΙT
    56-84-8, L-Aspartic acid, reactions 56-86-0, L-Glutamic acid,
                66-84-2, D-Glucosamine hydrochloride 70-18-8,
    reactions
    Glutathione, reactions 98-50-0 107-96-0, 3-Mercaptopropanoic
          498-40-8, L-Cysteic acid 598-21-0, Bromoacetyl bromide
                                     89889-52-1 123761-26-2
     6066-82-6, N-Hydroxysuccinimide
    148356-00-7 148356-01-8
                              172777-84-3, Cy 5.5
        (reaction; cell membrane impermeable arsenoxide compd. for
```

treating arthritis)

ANSWER 7 OF 28 HCA COPYRIGHT 2004 ACS on STN 137:165832 Activity based probe analysis. Patricelli, Matthew P. (Activx Biosciences, Inc., USA). PCT Int. Appl. WO 2002063271 A2 20020815, 62 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US3808 20020205. PRIORITY: US 2001-PV266687 20010205. AB The invention concerns methods and compns. are described for analyzing complex protein mixts. using fluorescent activity-based probes. In particular, probes that specifically react with and bind to the active form of one or more target proteins are employed. Fluorescent signals obtained from the labeled active target proteins can be related to the presence or amt. of active members of the desired target protein class. The methods and compns. described herein can be used, for example, to provide diagnostic information concerning pathogenic states, in identifying proteins that may act as therapeutic targets, and in drug discovery. 92-83-1, Xanthene ΙT (activity based probe anal.)

92-83-1 HCA

RN

CN

IC ICM GO1N CC9-14 (Biochemical Methods) Section cross-reference(s): 1, 14 Capillary electrophoresis ΙT Cyanine dyes Diagnosis Diffusion Drug screening Dyes Electrophoresis apparatus Fluorescent substances Fluorometry Functional groups

9H-Xanthene (9CI) (CA INDEX NAME)

Gel electrophoresis Labels

Mass spectrometry

Pathogen

Separation

(activity based probe anal.)

IT 91-64-5, Coumarin 92-83-1, Xanthene 7440-18-8D, Ruthenium, chelates 7440-27-9D, Terbium, chelates 7440-52-0D, Erbium, chelates 25168-10-9, Naphthylamine 138026-71-8, BODIPY (activity based probe anal.)

L99 ANSWER 8 OF 28 HCA COPYRIGHT 2004 ACS on STN

- 137:136908 Methods and means for detecting enzymatic cleavage and linkage reactions. Lopez-Calle, Eloisa; Fries, Joachim; Jungmann, Joern (Evotec OAI Ag, Germany). PCT Int. Appl. WO 2002059352 A2 20020801, 68 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2. APPLICATION: WO 2002-EP845 20020128. PRIORITY: EP 2001-101869 20010126.
- The invention relates to methods and means for detecting enzyme-catalyzed cleavage and linkage reactions. The invention provides modular chem. compds., which act as substrates for the enzymes concerned. The reaction products are detected using methods with a sensitivity to molar mass. Thus a Caspase 3-specific substrate was synthesized; first the substrate peptide was prepd. on a solid phase and coupled to 5-carboxytetramethylrhodamine succinimide ester. The product was modified with maleimide and conjugated to a 5'-thio modified double stranded DNA.

IT 444602-36-2P 444602-38-4P

(methods and means for detecting enzymic cleavage and linkage reactions)

RN 444602-36-2 HCA

CN L-Lysinamide, N-[[4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]cyclohexyl]carbonyl]glycyl-L-.alpha.-aspartyl-L-.alpha.-glutamyl-L-valyl-L-.alpha.-aspartylglycyl-N6-[4-[3,6-bis(dimethylamino)xanthylium-9-yl]-3-carboxybenzoyl]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

RN 444602-38-4 HCA

CN L-Lysinamide, N-[[4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]cyclohexyl]carbonyl]glycyl-L-isoleucyl-L-.alpha.-glutamyl-L-threonyl-L-.alpha.-aspartylglycyl-N6-[4-[3,6-bis(dimethylamino)xanthylium-9-yl]-3-carboxybenzoyl]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

IC ICM C12Q001-37

ICS C07K007-06

CC 7-1 (Enzymes)

Section cross-reference(s): 1

IT Carbohydrates, biological studies Dendritic polymers

Natural products

Nucleic acids

Peptides, biological studies Polymers, biological studies

Proteins

(methods and means for detecting enzymic cleavage and linkage reactions)

ΙT 9000-83-3, ATPase 9000-92-4, Amylase 9001-62-1, Lipase 9001-79-0, Phosphoamidase 9001-92-7, Protease 9012-56-0, Amidase 9012-90-2, DNA-polymerase 9012-96-8, Cysteine 9013-05-2, Phosphatase 9013-18-7, Acyl-CoA desulfhydrase synthetase 9014-19-1, Pyruvate carboxylase 9014-24-8, 9023-70-5, Glutamine synthetase RNA-polymerase Aldolase 9024-82-2, Pyrophosphatase 9026-81-7, Nuclease 9027-22-9, Decarboxylase 9027-34-3 9031-55-4, Carboxylase 9031-96-3, Peptidase 9032-92-2, Glycosidase 9044-86-4, 9047-25-0, Ammonia lyase 9068-67-1, Sulfatase Dehydratase 169592-56-7, Caspase-3

(methods and means for detecting enzymic cleavage and linkage reactions)

IT 444196-89-8P 444196-90-1P 444196-91-2P 444196-92-3P

444196-93-4P 444196-94-5P **444602-36-2P**

444602-38-4F

(methods and means for detecting enzymic cleavage and linkage reactions)

- L99 ANSWER 9 OF 28 HCA COPYRIGHT 2004 ACS on STN
- 137:17446 Rhodamine fluorophore useful as labeling reagent. Quiarelo, Ronald H.; Cheon, Liu Win; Yokobata, Kathy E. (Scinopharm Singapore Pte Ltd., Singapore). Jpn. Kokai Tokkyo Koho JP 2002168867 A2 20020614, 15 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 2000-355808 20001122.
- AR Rhodamine fluorophore and its compn. useful as a labeling reagent is provided, with which a substance such as amino acid, peptide, protein, nucleotide and nucleic acid is inexpensively and conveniently labeled in a stable state without lowering an efficiency. A fluorescent substance based on Rhodamine is derivatized, which forms a label-bound body capable of generating fluorescence upon irradiating light with an appropriate wavelength. A particularly preferable example is a certain single isomer of Rhodamine phosphoramidite. With these Rhodamine phosphoramidites, the efficiency in synthesizing a Rhodmine-labeled compd. by a solid phase method is stimulated. In this example of label-bound body, the conversion to non-fluorescent lactam is prevented due to the possession of a sufficiently substituted amide linkage derived from 3-carboxylic acid.
- IT 435304-72-6P 435304-73-7P

(Rhodamine fluorophore useful as labeling reagent)

- RN 435304-72-6 HCA
- CN Xanthylium, 3,6-bis(dimethylamino)-9-[2-[[[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutyl]methylamino]carbonyl]phenyl]- (9CI) (CA INDEX NAME)

RN 435304-73-7 HCA

CN Xanthylium, 3,6-bis(diethylamino)-9-[2-[[[2-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,4-dioxobutoxy]ethyl]methylamino]carbonyl]phenyl]-(9CI) (CA INDEX NAME)

IC ICM G01N033-533

ICS C12N015-09; C12Q001-02; C12Q001-68

CC 9-15 (Biochemical Methods)

IT Amide group

Amino group

Composition

Disulfide group

Fluorescence

Fluorescent substances

Light

Sulfhydryl group

Wavelength

(Rhodamine fluorophore useful as labeling reagent)

IT Amino acids, processes

Nucleic acids

Nucleotides, processes

Peptides, processes

Proteins

(Rhodamine fluorophore useful as labeling reagent)

IT 81-88-9DP, deriv. 81-88-9DP, phosphoramidite deriv.

L99 ANSWER 10 OF 28 HCA COPYRIGHT 2004 ACS on STN

136:101105 Membrane binding peptides of CD59 and DAF
derivatives in targeting lipid rafts of cell membranes for treatment
of inflammatory and immune disorders. Rowling, Pamela Jane
Elizabeth; Smith, Geoffrey Paul; Ridley, Simon Hugh (Adprotech
Limited, UK). PCT Int. Appl. WO 2002004638 A1 20020117, 51 pp.
DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR,
BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT,
BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR,

IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-GB3034 20010706. PRIORITY: GB

2000-16811 20000707. AB The present invention provides membrane binding elements assocd. with a sol. deriv. of complement regulatory polypeptides CD59 or DAF that bind lipid raft components for delivery of compds. to lipid rafts to modulate intracellular or extracellular activity. Hence, this invention can be used in the treatment of inflammatory and other immune disorders. A sol. deriv. of CD59 or DAF is provided which is assocd. With two or more heterologous membrane binding peptides with low membrane affinity. These membrane binding elements are sol. in ag. soln., and the elements are capable of interacting, independently and with thermodn. additivity with components of cellular or artificial membranes exposed to extracellular fluids. Specifically, the membrane binding elements target lipid raft components of the membrane and bind to the lipid rafts to localize the polypeptide at the lipid rafts. Thus, membrane binding elements mediate internalization of the proteins. Components of lipid rafts include one or more of phosphatidylserine, phosphatidyl glycerol, glycosphingolipids, cholesterol, GP1-anchored proteins assocd. with lipid rafts and other protein components of lipid rafts that may be found on the exo-plasmic cellular surface. Another embodiment of the invention provides sol. derivs. which include a derivatized antibody or antibody fragment which can provide a surrogate receptor localized at a lipid raft to divert a mediator interacting with a lipid raft receptor or which can neutralize a cofactor of the raft needed for signaling. derivs. also include chem. or biol. compds. that have fluorescent

properties or compds. that can form chem. bonds with proteins, sugar groups or lipids with crosslinking groups, enzymes, enzyme substrates or inhibitors and are used to study patching behavior of membrane proteins and lipids in DIGs. Sol. proteins of the present invention can be linked to membrane binding elements by disulfide bonds. Sol. forms of proteins that are normally located in lipid rafts can be produced either by recombinant methods or isolated from human urine or plasma. These proteins can be treated with 2-iminothiolane and further reacted with a pyridylthio group linked to the membrane binding peptide. The membrane binding peptide may also be linked to the sol. protein by a C-terminal cysteine in the sol. protein.

IT 52-90-4, Cysteine, biological studies

(C-terminal, in CD59 and DAF proteins, for linkage to membrane peptides; membrane binding peptides of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

RN 52-90-4 HCA

CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 387847-69-0 387847-73-6 388621-69-0 388621-72-5 388621-75-8

(lipid-raft targeting using; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

RN 387847-69-0 HCA

CN Benzoic acid, 2,3,5-trichloro-4-[[[5-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)pentyl]amino]carbonyl]-6-(1,3,4,8,9,10-hexahydro-2,2,4,8,10,10-hexamethyl-12,14-disulfo-2H-pyrano[3,2-g:5,6-g']diquinolin-6-yl)- (9CI) (CA INDEX NAME)

RN 387847-73-6 HCA

CN L-Cysteinamide, N-(1-oxotetradecyl)glycyl-L-seryl-L-seryl-L-lysyl-L-seryl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-seryl-L-lysyl-L

Absolute stereochemistry.

PAGE 1-C

RN 388621-69-0 HCA

CN Xanthylium, 3,6-diamino-9-[2-carboxy-4(or 5)-[[[5-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)pentyl]amino]carbonyl]phenyl]-4,5-disulfo-, inner salt (9CI) (CA INDEX NAME)

RN 388621-72-5 HCA

CN L-Cysteinamide, N-(1-oxotetradecyl)glycyl-L-seryl-L-seryl-L-lysyl-L-seryl-L-lysyl-L

PAGE 1-A

PAGE 3-A

PAGE 4-A

RN 388621-75-8 HCA

L-Cysteinamide, N-(1-oxotetradecyl)glycyl-L-seryl-L-seryl-L-lysyl-L-seryl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-seryl-L-lysyl-

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

$$H_{2N}$$
 H_{2N}
 H_{2N}

PAGE 1-C

PAGE 1-D

(CH₂)₄ | O

PAGE 2-C

IC ICM C12N015-12 ICS C07K014-705; C07C323-41; C07C323-59; A61K047-48

CC 15-4 (Immunochemistry)
Section cross-reference(s): 3, 6, 14

membrane binding peptide soluble complement regulator CD59
DAF deriv; targeting lipid raft deriv CD59 DAF; treatment immune inflammatory disorder lipid raft deriv CD59 DAF; fusion protein membrane binding peptide DAF; CD59 fusion protein membrane binding peptide; CR1 receptor fusion protein membrane binding peptide

IT Signal transduction, biological (CD59 and DAF derivs. in cell membrane lipid rafts in; membrane

binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Carbohydrates, biological studies

Lipids, biological studies

Proteins

(CD59 and DAF peptide variants crosslinked by; membrane binding peptides of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Brain

(DAF from, human; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Glycosphingolipids

Phosphatidylglycerols

Phosphatidylserines

(as lipid raft component; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders).

IT Immunity

(disorder, treatment of; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Crosslinking agents

(enzyme-activated, covalent bonds with **proteins**, sugars or lipids in lipid rafts formed by; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Body fluid

(extracellular, lipid rafts interacting with mols. from; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Chimeric gene

(for CD59 and DAF fusion products with membrane binding peptides; membrane binding peptides of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Urine

(human, sol. CD59 from; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Enzymes, biological studies

(inhibitors, lipid raft targeting using; membrane binding peptides of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune

disorders)

IT Biological transport

(intracellular; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Confocal laser scanning microscopy

(lipid raft targeting visualized using; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Organelle

(lipid raft, in cell membrane; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Lysosome

(lipid raft-membrane targeting complexes in; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Fluorescence microscopy

(lipid raft-targeting complexes detected by; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Cell membrane

(membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Antibodies

(monoclonal, to CD59 or DAF derivs., fluorescent labeled, fragments of; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT **Protein** sequences

(of CD59 and DAF derivs. of human; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Post-translational processing

(of CD59 and DAF derivs. to link membrane binding peptides; membrane binding peptides of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Protein engineering

(of CD59 and DAF derivs.; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Molecular cloning

(of CD59 and DAF sol. derivs.; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Glycolipoproteins

(phosphatidylinositol-contg., in lipid rafts; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Crosslinking agents

(photochem., covalent bonds with **proteins**, sugars or lipids in lipid rafts formed by; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT CD59 (antigen)

(sol. derivs., fusion proteins, in lipid rafts,; membrane binding peptides of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Enzymes, biological studies

(substrates for, lipid raft targeting using; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Antibodies

(to CD59 or DAF derivs., fluorescent labeled, fragments of; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Inflammation

(treatment of; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT Complement receptors

(type 1, fusion **proteins**; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

1T 388635-55-0 388635-56-1 388635-57-2 388635-58-3 (amino acid sequence; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT 57-88-5, Cholesterol, biological studies

(as lipid raft component; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

TT 75350-46-8, Fluorescein-5-maleimide 387847-69-0 387847-71-4 387847-73-6 388621-69-0

388621-72-5 388621-75-8

(lipid-raft targeting using; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT 56-81-5, Glycerol, reactions 5961-85-3, Tris-2-carboxyethyl phosphine 6539-14-6, 2-Iminothiolane 143379-89-9 (sol. GPI proteins linked to membrane binding peptides using; membrane binding peptides of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT 99085-47-9D, DAF, fusion proteins (sol. derivs. of; membrane binding peptides of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT 37758-47-7, Ganglioside GM1
 (subunit B, as lipid-raft marker, fluorescent label on; membrane
 binding peptides of CD59 and DAF derivs. in targeting
 lipid rafts of cell membranes for treatment of inflammatory and
 immune disorders)

IT 388649-87-4 388649-88-5 388649-89-6 388649-90-9 388649-91-0 388649-92-1

(unclaimed **protein** sequence; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

IT 202519-63-9

(unclaimed sequence; membrane binding **peptides** of CD59 and DAF derivs. in targeting lipid rafts of cell membranes for treatment of inflammatory and immune disorders)

L99 ANSWER 11 OF 28 HCA COPYRIGHT 2004 ACS on STN

135:352306 Identification and reactivity of the major metabolite
 (.beta.-1-glucuronide) of the anti-tumor agent 5,6 dimethylxanthenone-4-acetic acid (DMXAA) in humans. Zhou, S. F.;
 Paxton, J. W.; Tingle, M. D.; Kestell, P.; Jameson, M. B.; Thompson,
 P. I.; Baguley, B. C. (Department of Pharmacology and Clinical
 Pharmacology, University of Auckland, Auckland, N. Z.).
 Xenobiotica, 31(5), 277-293 (English) 2001. CODEN: XENOBH. ISSN:
 0049-8254. Publisher: Taylor & Francis Ltd..

AB The novel antitumor agent 5,6-dimethylxanthenone-4-acetic acid (DMXAA) is extensively metabolized by glucuronidation and 6-methylhydroxylation, resulting in DMXAA acyl glucuronide (DMXAA-G) and 6-hydroxymethyl-5-methylxanthenone-4-acetic acid (6-OH-MXAA).

The major human urinary metabolite of DMXAA was isolated and purified by a solid-phase extn. (SPE) method. The isolated metabolite was hydrolyzed to free DMXAA by strong base, and by .beta.-glucuronidase. Liq. chromatog.-mass spectrometry (LC-MS) and spectral data indicated the presence of a mol. ion [M + 1]+ at m/z 459, which was consistent with the mol. wt. of protonated DMXAA-G. The glucuronide was unstable in buffer at physiol. pH, plasma and blood with species variability in half-life. Hydrolysis and intramol. migration were major degrdn. pathways. In vitro and in vivo formation of DMXAA-protein adducts was obsd. The formation of DMXAA-protein adducts in cancer patients receiving DMXAA was significantly correlated with plasma DMXAA-G concn. and max. plasma DMXAA concn. At least five metabolites of DMXAA were obsd. in patient urine, with up to 60% of the total dose excreted as DMXAA-G, 5.5% as 6-OH-MXAA and 4.5% as the glucuronide of 6-OH-MXAA. These data suggest that the major metabolite in patients' urine is DMXAA .beta.-1-glucuronide, which may undergo hydrolysis, mol. rearrangement and covalent binding to plasma protein. The reactive properties of DMXAA-G may have important implications for the pharmacokinetics, pharmacodynamics and toxicity of DMXAA. 117570-53-3D, 5,6-Dimethylxanthenone-4-acetic acid, protein adducts 162070-60-2, 5,6-Dimethylxanthenone-4-acetic acid acyl glucuronide 162070-60-2D, 5,6-Dimethylxanthenone-4-acetic acid acyl

372941-08-7D, protonated metabolite (identification and reactivity of the major metabolite of the antitumor agent 5,6-dimethylxanthenone-4-acetic acid in humans)

RN 117570-53-3 HCA

ΙΤ

CN 9H-Xanthene-4-acetic acid, 5,6-dimethyl-9-oxo- (9CI) (CA INDEX NAME)

glucuronide isomer, protonated metabolite 223261-32-3,

6-Hydroxymethyl-5-methylxanthenone-4-acetic acid 372941-08-7, 6-Hydroxymethyl-5-methylxanthenone-4-acetic acid glucuronide

RN 162070-60-2 HCA

CN .beta.-D-Glucopyranuronic acid, 1-(5,6-dimethyl-9-oxo-9H-xanthene-4-

acetate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 162070-60-2 HCA

cN .beta.-D-Glucopyranuronic acid, 1-(5,6-dimethyl-9-oxo-9H-xanthene-4-acetate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 223261-32-3 HCA

CN 9H-Xanthene-4-acetic acid, 6-(hydroxymethyl)-5-methyl-9-oxo- (9CI) (CA INDEX NAME)

RN 372941-08-7 HCA

CN .beta.-D-Glucopyranosiduronic acid, [5-(carboxymethyl)-4-methyl-9-oxo-9H-xanthen-3-yl]methyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 372941-08-7 HCA

CN .beta.-D-Glucopyranosiduronic acid, [5-(carboxymethyl)-4-methyl-9-oxo-9H-xanthen-3-yl]methyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.

CC 1-2 (Pharmacology)

117570-53-3D, 5,6-Dimethylxanthenone-4-acetic acid, protein adducts 162070-60-2, 5,6-Dimethylxanthenone-4-acetic acid acyl glucuronide 162070-60-2D, 5,6-Dimethylxanthenone-4-acetic acid acyl glucuronide isomer, protonated metabolite 223261-32-3, 6-Hydroxymethyl-5-methylxanthenone-4-acetic acid 372941-08-7, 6-Hydroxymethyl-5-methylxanthenone-4-acetic acid glucuronide 372941-08-7D, protonated metabolite (identification and reactivity of the major metabolite of the antitumor agent 5,6-dimethylxanthenone-4-acetic acid in humans)

L99 ANSWER 12 OF 28 HCA COPYRIGHT 2004 ACS on STN

135:238927 Silver and gold colloidal particle coating based optical sensors for biomolecule detection. Carron, Keith T.; Corcoran, Robert C.; Sulk, Roberta A. (University of Wyoming, USA). PCT Int. Appl. WO 2001071353 Al 20010927, 75 pp. DESIGNATED STATES: W: CA, JP, MX; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US6357 20010228. PRIORITY: US 2000-527226 20000316.

AB A colloidal system for detection of a variety of applytos is

AB A colloidal system for detection of a variety of analytes is described which involves techniques which permit reconstitution of a desiccated substance such as for surface enhanced Raman spectroscopic anal. and multiple sensors at once, each having different spectra through the use of markers or the like. Competitive assay techniques and a variety of substances are described which provides a practical and versatile system which can also be used for immunol. assays and can include antibodies tagged to provide spectroscopic indicia.

IT 92-83-1, Xanthene

(silver and gold colloidal particle coating based optical sensors for biomol. detection)

92-83-1 HCA RN 9H-Xanthene (9CI) (CA INDEX NAME) CN

G01N033-543 IC ICM

9-1 (Biochemical Methods) CC

Section cross-reference(s): 2, 4, 15

Alcohols, analysis ΤТ

Hormones, animal, analysis

Neurotransmitters

Phenols, analysis

Prostate-specific antigen

Proteins, general, analysis

(silver and gold colloidal particle coating based optical sensors for biomol. detection)

Polyoxyalkylenes, uses ΙT

(silver and gold colloidal particle coating based optical sensors for biomol. detection)

84-65-1, Anthraquinone 91-64-5, Coumarin **92-83-1**, ΙΤ

Xanthene 94-75-7, 2,4-Dichlorophenoxyacetic acid, uses 574-93-6, Phthalocyanine 574-93-6D, Phthalocyanine, derivs. 1563-66-2, Carbofuran

(silver and gold colloidal particle coating based optical sensors for biomol. detection)

7664-38-2D, phosphoric acid, derivs., uses 7664-93-9, Sulfuric ΙT acid, uses 9002-84-0, Teflon 13598-36-2D, phosphonic acid, 25322-68-3, Polyethylene glycol

(silver and gold colloidal particle coating based optical sensors for biomol. detection)

ANSWER 13 OF 28 HCA COPYRIGHT 2004 ACS on STN L99

134:261272 Cell membrane-impermeable arsenoxide compounds, their preparation, pharmaceutical compositions, and therapeutic and diagnostic use. Hogg, Philip John; Donoghue, Neil (Unisearch Limited, Australia). PCT Int. Appl. WO 2001021628 A1 20010329, 122 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-AU1143 20000920. PRIORITY: AU 1999-2967 19990920.

- The invention discloses compds. A(LY)p, (A = .gtoreq.1 substantially cell-membrane impermeable pendant group; L = linker and/or spacer; Y = .gtoreq.1 arsenoxide or arsenoxide equiv.; p = 1-10; sum total of C atoms in A and L together >6). Prepn. of e.g. 4-[N-(S-glutathionylacetyl)amino]phenylarsenoxide is described, as are e.g. the antitumor activity, tumor imaging ability, and activity inhibiting HIV infection of compds. of the invention. Pharmaceutical formulations are also described.
- RN 148356-00-7 HCA
 CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-5-carboxamide,
 N-[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]-3',6'-dihydroxy-3oxo- (9CI) (CA INDEX NAME)

- RN 148356-01-8 HCA
 CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-6-carboxamide,
 N-[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]-3',6'-dihydroxy-3oxo- (9CI) (CA INDEX NAME)
- N— O— C— (CH₂) 5— NH— C

- ICM C07F009-20 IC C07F009-78; C07F009-74 ICS
- 1-12 (Pharmacology) CC Section cross-reference(s): 29, 63
- Amines, biological studies ΙT Amino acids, biological studies Oligosaccharides, biological studies Peptides, biological studies

Proteins, general, biological studies Radionuclides, biological studies

Transition metals, biological studies

(arsenoxide derivs.; substantially cell membrane-impermeable compd. and use thereof)

- Proteins, specific or class ΙΤ (mercapto-contg., arsenoxide derivs.; substantially cell membrane-impermeable compd. and use thereof)
- 56-86-0, L-Glutamic acid, 56-84-8, L-Aspartic acid, reactions ΙT 66-84-2, D-Glucosamine hydrochloride 70-18-8, 98-50-0, p-Arsanilic acid 107-96-0, Glutathione, reactions 3-Mercaptopropanoic acid 498-40-8, L-Cysteic acid 598-21-0, 6066-82-6, N-Hydroxysuccinimide 67278-31-3 Bromoacetyl bromide 123740-08-9 148356-00-7 148356-01-8 89889-52-1 172777-84-3, Cy5.5

(reaction; substantially cell membrane-impermeable compd. and use thereof)

- 37318-49-3, Protein disulfide isomerase ΙT (substantially cell membrane-impermeable compd. and use thereof)
- ANSWER 14 OF 28 HCA COPYRIGHT 2004 ACS on STN
- 134:141330 Identification of the human liver cytochrome P450 isoenzyme responsible for the 6-methylhydroxylation of the novel anticancer drug 5,6-dimethylxanthenone-4-acetic acid. Zhou, Shufeng; Paxton, James W.; Tingle, Malcolm D.; Kestell, Philip (Department of Pharmacology and Clinical Pharmacology, The University of Auckland, Auckland, N. Z.). Drug Metabolism and Disposition, 28(12), 1449-1456 (English) 2000. CODEN: DMDSAI. ISSN: 0090-9556. Publisher: American Society for Pharmacology and Experimental Therapeutics.
- In vitro studies were conducted to identify the hepatic cytochrome P AΒ 450 (CYP) isoenzyme involved in the 6-methylhydroxylation of 5,6-dimethylxanthenone-4-acetic acid (DMXAA) by using a human liver library (n = 14). The metabolite 6-hydroxymethyl-5-methylxanthenone-4-acetic acid (6-OH-MXAA) was detd. by HPLC with fluorescence detection. The metabolite formed in human liver microsomes and by cDNA-expressed CYP isoform was identified by liq. chromatog.

mass spectrometry as 6-OH-MXAA. In human liver microsomes (n = $\overline{14}$), 6-methylhydroxylation of DMXAA followed monophasic Michaelis-Menten kinetics, with a mean apparent Km of 21

.+-. 5 .mu.M and Vmax of 0.043 .+-. 0.019 nmol/min/mg. An approx. 10-fold interindividual variation in the intrinsic clearance (Vmax/Km) of DMXAA 6-methylhydroxylation in human liver microsomes was obsd. The involvement of CYP1A2 in DMXAA metab. by human livers was demonstrated by the following: 1) the potent inhibition of DMXAA metab. by furafylline (kinact = 0.23 .+-. 0.04 min-1, K'app = 15.6.+-. 6.7 .mu.M) and .alpha.-naphthoflavone (Ki = 0.036 .mu.M), but not by cimetidine, ketoconazole, tolbutamide, quinidine, chlorzoxazone, diethyldithiocarbamate, troleandomycin, and sulfaphenazole; 2) when incubated with human lymphoblastoid cell microsomes contg. cDNA-expressed CYP isoenzymes, DMXAA was metabolized only by CYP1A2, with an apparent Km of 6.2 .+-. 1.5 .mu.M and Vmax of 0.014 .+-. 0.001 nmol/min/mg, but not by CYP2A6, CYP2B6, CYP2C9 (Arg144), CYP2C19, CYP2D6 (Val374), CYP2E1, and CYP3A4; 3) a significant correlation (r = 0.90; P < .001) between 6-methylhydroxylation of DMXAA and 7-ethoxyresorufin O-deethylation; and 4) a significant correlation (r = 0.75; P < .01) between the CYP1A protein level detd. by Western blots and DMXAA 6-methylhydroxylation.

117570-53-3, 5,6-Dimethylxanthenone-4-acetic acid ΙT (human liver cytochrome P 450 isoenzyme responsible for methylhydroxylation of dimethylxanthenoneacetic acid)

117570-53-3 HCA RN

9H-Xanthene-4-acetic acid, 5,6-dimethyl-9-oxo- (9CI) (CA INDEX CNNAME)

ΙT 223261-32-3

(human liver cytochrome P 450 isoenzyme responsible for methylhydroxylation of dimethylxanthenoneacetic acid)

223261-32-3 HCA RN

9H-Xanthene-4-acetic acid, 6-(hydroxymethyl)-5-methyl-9-oxo- (9CI) CN (CA INDEX NAME)

CC 1-2 (Pharmacology)

117570-53-3, 5,6-Dimethylxanthenone-4-acetic acid (human liver cytochrome P 450 isoenzyme responsible for methylhydroxylation of dimethylxanthenoneacetic acid)

IT 223261-32-3

(human liver cytochrome P 450 isoenzyme responsible for methylhydroxylation of dimethylxanthenoneacetic acid)

L99 ANSWER 15 OF 28 HCA COPYRIGHT 2004 ACS on STN

134:27295 Methods for producing 5'-nucleic acid-protein
conjugates. Lohse, Peter; Wright, Martin C.; McPherson, Michael
(Phylos, Inc., USA). PCT Int. Appl. WO 2000072869 A1 20001207, 32
pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG,
BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO,
RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF,
CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC,
ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2.
APPLICATION: WO 2000-US15077 20000601. PRIORITY: US 1999-PV137032
19990601.

Disclosed herein is a method for generating a 5'-nucleic acid-AΒ protein conjugate, the method involving: (a) providing a nucleic acid which carries a reactive group at its 5'end; (b) providing a non-derivatized protein; and (c) contacting the nucleic acid and the protein under conditions which allow the reactive group to react with the N-terminus of the protein, thereby forming a 5'-nucleic acid-protein conjugate. In one approach, fusions are formed by reaction between an unprotected protein carrying an N-terminal cysteine and a nucleic acid carrying a 1,2-aminothiol reactive group. In a second approach, fusion formation occurs as the result of a biarsenical-tetracysteine interaction. Also disclosed herein are 5'-nucleic acid-protein conjugates and methods for their use in (1) the selection of a desired nucleic acid or a desired protein by sepg. the

binding partner-candidate conjugate complex from unbound members of a population, and (2) detecting an interaction between a protein and a compd.

IT 311797-39-4P

(methods for producing 5'-nucleic acid-protein conjugates)

RN 311797-39-4 HCA

CN Benzenebutanamide, N-[3-[[4',5'-bis(1,3,2-dithiarsolan-2-yl)-3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl]amino]-3-oxopropyl]-4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)- (9CI) (CA INDEX NAME)

IT 52-90-4, L-Cysteine, reactions

(reaction with nucleic acid carrying a 1,2-aminothiol reactive group; methods for producing 5'-nucleic acid-protein conjugates)

RN 52-90-4 HCA

CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IC ICM A61K038-16

ICS A61K038-03; C07K014-00

CC 9-16 (Biochemical Methods)

Section cross-reference(s): 33, 34

```
ST
     nucleic acid conjugate protein
     Thiols (organic), reactions
ΙT
        (amino, nucleic acids contg., reaction with N-terminal cysteinyl
        proteins; methods for producing 5'-nucleic acid-
        protein conjugates)
TΤ
     DNA
     Nucleic acids
       Proteins, specific or class
     RNA
     mRNA
        (conjugates; methods for producing 5'-nucleic acid-
        protein conjugates)
ΙΤ
     Nucleoproteins
        (methods for producing 5'-nucleic acid-protein
        conjugates)
IT
     Amines, reactions
        (thiol, nucleic acids contg., reaction with N-terminal cysteinyl
        proteins; methods for producing 5'-nucleic acid-
        protein conjugates)
     56377-57-2
ΙT
        (methods for producing 5'-nucleic acid-protein
        conjugates)
     311797-38-3P 311797-39-4P
ΙΤ
        (methods for producing 5'-nucleic acid-protein
        conjugates)
ΙT
     52-90-4, L-Cysteine, reactions
        (reaction with nucleic acid carrying a 1,2-aminothiol reactive
        group; methods for producing 5'-nucleic acid-protein
        conjugates)
                    312323-66-3
                                  312323-67-4
                                                 312343-85-4
ΙT
     312323-65-2
        (unclaimed sequence; methods for producing 5'-nucleic acid-
        protein conjugates)
    ANSWER 16 OF 28 HCA COPYRIGHT 2004 ACS on STN
134:500 Method for activity profiling compound mixtures. Pidgeon,
     Charles; Rooke, Nadege M.; Ruell, Jeffrey A. (Admetric Biochem Inc.,
     USA). PCT Int. Appl. WO 2000070344 A2 20001123, 84 pp. DESIGNATED
     STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH,
     CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
     HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
     LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG,
     SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ,
     BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM,
     CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO
     2000-US13178 20000512. PRIORITY: US 1999-PV133968 19990513.
```

A method is described for identifying compds. in a complex mixt.

exhibiting a predetd. characteristic. The mixt. is sepd. into

AΒ

fractions using at least two unique sets of sepn. parameters to produce at least two series of sepn. parameter dependent fractions. In one embodiment the mixts. are sepd. chromatog. using unique sets of sepn. parameters and the fractions are analyzed spectroscopically to provided data indicative of the component compds. and the fractions are either analyzed individually, or in synchronously combined fractions, for the predetd. characteristic. The spectroscopic data for the fractions exhibiting the predetd. characteristic are compared to identify compd.(s) common to the fractions exhibiting the characteristic. The method can be implemented in an automatic chromatog. system to provide rapid screening of complex compd. mixts. for predetd. chem. or biol. characteristics and to identify those components of the mixt. exhibiting such characteristics. The invention can be applied to the rapid and efficient collection of databases of chromatog. fingerprints for large compd. libraries and seems perfectly suited for lead identification and optimization of chem. libraries, which is a very important aspect of the drug discovery process, as well as QSAR studies.

IT 298-50-0, Propantheline

(activity profiling of compd. mixts.)

RN 298-50-0 HCA

و َ ق

CN 2-Propanaminium, N-methyl-N-(1-methylethyl)-N-[2-[(9H-xanthen-9-ylcarbonyl)oxy]ethyl]- (9CI) (CA INDEX NAME)

IC ICM G01N033-53

CC 1-1 (Pharmacology)

Section cross-reference(s): 9

IT Mass spectrometry

(HPLC combined with; activity profiling of compd. mixts.)

IT Chromatography

Combinatorial library

Drug screening

HPLC

IR spectroscopy

Mass spectrometry

NMR spectroscopy

Separation

Spectroscopy

Toxicity UV and visible spectroscopy (activity profiling of compd. mixts.) Natural products ΤТ Protein hydrolyzates Proteins, general, analysis (activity profiling of compd. mixts.) HPLC ΙT (mass spectrometry combined with; activity profiling of compd. mixts.) 51-55-8, Atropine, analysis 52-86-8, 50-49-7, Imipramine ΙT 54-04-6, Mescaline 54-05-7, Chloroquine 54-30-8, Haloperidol 58-25-3, Chlordiazepoxide 58-73-1, Diphenhydramine Camylofin 59-32-5, Chloropyramine 59-98-3, Tolazoline 59-26-7, Nikethamide 77-23-6, Carbetapentane 64-95-9, Adiphenine 68-88-2, Hydroxyzine 83-98-7, Orphenadrine 77-37-2, Procyclidine 82-92-8, Cyclizine 86-22-6, Brompheniramine 91-75-8, Antazoline 91-80-5, 92-12-6, Phenyltoloxamine 93-30-1, Methapyrilene 99-43-4, Benoxinate 125-53-1, Oxyphencyclimine Methoxyphenamine 132-22-9, Chlorpheniramine 144-11-6 130-95-0, Quinine **298-50-0,** Propantheline 299-42-3, Ephedrine 439-14-5, Diazepam 486-47-5, Ethaverine 512-15-2, Cyclopentolate 586-60-7, Dyclonine 636-54-4, Clopamide 642-72-8, Benzydamine 1491-59-4, Oxymetazoline 1508-75-4, Tropicamide 1668-19-5, 2898-12-6, 2086-83-1, Berberine 1977-10-2, Loxapine Doxepin 5053-06-5, 3820-67-5, Glafenine 2955-38-6, Prazepam Medazepam 5845-26-1, Thiazesim Fenspiride 5633-20-5, Oxybutynin 13392-18-2, Fenoterol 12794-10-4D, Benzodiazepine, derivs. 14051-33-3, Benzetimide 14214-84-7, 13655-52-2, Alprenolol 18559-94-9, Salbutamol 17617-23-1, Flurazepam Oxyphenonium 21888-98-2, Dexetimide 23256-50-0, Guanabenz acetate 34368-04-2, 30516-87-1, AZT 26839-75-8, Timolol Mianserin 37148-27-9, Clenbuterol 36894-69-6, Labetalol Dobutamine 37517-30-9, Acebutolol 40796-97-2 41094-88-6, Tracazolate 42399-41-7, Diltiazem 50679-08-8, Terfenadine 51264-14-3, 54143-55-4, Flecainide 54063-53-5, Propafenone 57149-07-2, Naftopidil 60205-81-4, Ipratropium 65277-42-1, Ketoconazole 70458-96-7, Norfloxacin 82626-48-0, Zolpidem 84371-65-3, Mifepristone (activity profiling of compd. mixts.) ANSWER 17 OF 28 HCA COPYRIGHT 2004 ACS on STN 133:361699 A diverse set of oligomeric class II MHC-peptide complexes for probing T-cell receptor interactions. Cochran, Jennifer R.; Stern, Lawrence J. (Department of Chemistry,

Massachusetts Institute of Technology, Cambridge, MA, 02139, USA). Chemistry & Biology, 7(9), 683-696 (English) 2000. CODEN: CBOLE2.

ISSN: 1074-5521. Publisher: Elsevier Science Ltd.. Background: T-cells are activated by engagement of their clonotypic cell surface receptors with peptide complexes of major histocompatibility complex (MHC) proteins, in a poorly understood process that involves receptor clustering on the membrane surface. Few tools are available to study the mol. mechanisms responsible for initiation of activation processes in T-cells. Results: A topol. diverse set of oligomers of the human MHC protein HLA-DR1, varying in size from dimers to tetramers, was produced by varying the location of an introduced cysteine residue and the no. and spacing of sulfhydryl-reactive groups carried on novel and com. available crosslinking reagents. Fluorescent probes incorporated into the crosslinking reagents facilitated measurement of oligomer binding to the T-cell surface. Oligomeric MHC-peptide complexes, including a variety of MHC dimers, trimers and tetramers, bound to T-cells and initiated T-cell activation processes in an antigen-specific manner. Conclusion: T-cell receptor dimerization on the cell surface is sufficient to initiate intracellular signaling processes, as a variety of MHC-peptide dimers differing in intramol. spacing and orientation were each able to trigger early T-cell activation events. The relative binding affinities within a homologous series of MHC-peptide oligomers suggest that T-cell receptors may rearrange in the plane of the membrane concurrent with oligomer binding.

272788-73-5 272789-77-2 ΙT

(for prepn. of oligomeric class II MHC-peptide complexes)

272788-73-5 HCA RN

AB

Glycinamide, N-[[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-CN[9H]xanthen]-5-yl)amino]thioxomethyl]-.beta.-alanyl-L-.alpha.glutamyl-N6-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-Llysyl-L-serylglycyl-L-seryl-N6-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1yl)-1-oxohexyl]-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

RN 272789-77-2 HCA CN Glycinamide, N-[[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'- [9H]xanthen]-5-yl)amino]thioxomethyl]-.beta.-alanyl-L-.alpha.-glutamyl-N6-[6-[[4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]cyclohexyl]carbonyl]amino]-1-oxohexyl]-L-lysyl-L-serylglycyl-L-serylglycyl-N6-[6-[[[4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]cyclohexyl]carbonyl]amino]-1-oxohexyl]-L-lysyl-L-serylglycyl-L-.alpha.-glutamyl-L-seryl-N6-[6-[[[4-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]cyclohexyl]carbonyl]amino]-1-oxohexyl]-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

CC 15-1 (Immunochemistry)

ST oligomer MHC peptide complex T cell activation; TCR

receptor interaction oligomer MHC peptide complex

IT TCR .alpha..beta. (receptor)

TCR .alpha..beta. (receptor)

(CD3 complex; oligomeric class II MHC-peptide complexes for probing T-cell activation via)

ΙΤ Histocompatibility antigens (HLA-DR1, complexes, with antigenic peptides; antigen-specific T-cell activation in response to oligomers of) ΙT Cell activation (T cell; by oligomeric class II MHC-peptide complexes) CD3 (antigen) ITCD3 (antigen) (TCR .alpha..beta. complex; oligomeric class II MHCpeptide complexes for probing T-cell activation via) T cell (lymphocyte) IT(activation; by oligomeric class II MHC-peptide complexes) IT Peptides, biological studies (complexes, complexes, with HLA-DR1; antigen-specific T-cell activation in response to oligomers of) ΙΤ 272788-73-5 272789-77-2 272789-78-3 (for prepn. of oligomeric class II MHC-peptide complexes) ANSWER 18 OF 28 HCA COPYRIGHT 2004 ACS on STN 133:172215 Controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element. Kenten, John H.; Roberts, Steven F.; Lebowitz, Michael S. (Proteinix, Inc., USA). PCT Int. Appl. WO 2000047220 Al 20000817, 106 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US3436 20000211. PRIORITY: US 1999-PV119851 19990212; US 1999-406781 19990928. The invention relates to novel compds, comprising a ubiquitination ABrecognition element and a protein binding element. invention also relates to the use of said compds. for modulating the level and/or activity of a target protein. The compds. are useful for the treatment of diseases such as infections, inflammatory conditions, cancer and genetic diseases. The compds. are also useful as insecticides and herbicides. 288257-29-4 ΙΤ (fluorescein antibodies targeted degrdn. stimulation by; controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element and use as drugs and pesticides)

RN

288257-29-4 HCA

CN L-Cysteine, L-arginyl-6-aminohexanoyl-S-[1-(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)-2,5-dioxo-3-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

- IC ICM A61K038-00
- CC 1-12 (Pharmacology)

 Section cross-reference(s): 5

Section cross-reference(s): 5

ST protein control ubiquitination recognition element; pharmacol protein control ubiquitination recognition element; pesticide protein control

ubiquitination recognition element; insecticide protein control ubiquitination recognition element; herbicide protein control ubiquitination recognition element

IT Protein motifs

(Deg1, ubiquitination recognition element binding to; controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element)

IT Protein motifs

(Deg2, ubiquitination recognition element binding to; controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element)

IT Histocompatibility antigens

(MHC (major histocompatibility complex), class I, targeted degrdn. of; controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element and use as drugs and pesticides)

IT Histocompatibility antigens

(MHC (major histocompatibility complex), class II, targeted degrdn. of; controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element and use as drugs and pesticides)

IT Histocompatibility antigens

(MHC (major histocompatibility complex), targeted degrdn. of; controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element and use as drugs and pesticides)

IT Protein motifs

(N-end N-recognin, ubiquitination recognition element binding to; controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element)

IT Protein motifs

(PEST motif, ubiquitination recognition element binding to; controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element)

IT Protein motifs

(WW domain, ubiquitination recognition element binding to; controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element)

IT Anti-AIDS agents

Anti-infective agents Antitumor agents Antiviral agents Parasiticides Pesticides

Protein degradation

(controlling **protein** levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a **protein** binding element and use as drugs and pesticides)

IT Peptides, biological studies

(controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element and use as drugs and pesticides)

IT Proteins, general, biological studies

(controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element and use as drugs and pesticides)

IT Protein motifs

(delta domain, ubiquitination recognition element binding to; controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element)

IT Protein motifs

(destruction box, ubiquitination recognition element binding to; controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element)

IT Protein motifs

(phosphorylated sequences, ubiquitination recognition element binding to; controlling **protein** levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a **protein** binding element)

IT Antigens

Thioredoxins

(targeted degrdn. of; controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element and use as drugs and pesticides)

IT Antibodies

(to fluorescein, targeted degrdn. of; controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element and use as drugs and pesticides)

IT Cytomegalovirus Hepatitis A virus

```
Hepatitis B virus
     Hepatitis C virus
     Hepatitis GB virus C/G
     Human herpesvirus
     Human immunodeficiency virus 1
     Human immunodeficiency virus 2
     Rabies virus
     Rous sarcoma virus
        (treatment of infection with; controlling protein
        levels in eucaryotic organisms using novel compds. comprising a
        ubiquitination recognition element and a protein
        binding element and use as drugs and pesticides)
ΙΤ
     Enzymes, biological studies
        (ubiquitin-conjugating; controlling protein levels in
        eucaryotic organisms using novel compds. comprising a
        ubiquitination recognition element and a protein
        binding element and use as drugs and pesticides)
ΙΤ
     Hepatitis
        (viral, treatment of; controlling protein levels in
        eucaryotic organisms using novel compds. comprising a
        ubiquitination recognition element and a protein
        binding element and use as drugs and pesticides)
ΙT
     288257-27-2
        (HIV integrase targeted degrdn. stimulation by; controlling
        protein levels in eucaryotic organisms using novel
        compds. comprising a ubiquitination recognition element and a
        protein binding element and use as drugs and pesticides)
     52350-85-3, Integrase
ΙT
        (HIV, targeted degrdn. of; controlling protein levels
        in eucaryotic organisms using novel compds. comprising a
        ubiquitination recognition element and a protein
        binding element and use as drugs and pesticides)
ΙT
     2321-07-5, Fluorescein
        (antibodies to, targeted degrdn. of; controlling protein
        levels in eucaryotic organisms using novel compds, comprising a
        ubiquitination recognition element and a protein
        binding element and use as drugs and pesticides)
ΙT
     28971-77-9D, linker derivs.
                                   112558-12-0D, linker derivs.
     288256-96-2
                   288256-97-3
                                 288256-98-4
                                               288256-99-5
                                                             288257-00-1
                                 288257-03-4
                                               288257-04-5
     288257-01-2
                   288257-02-3
                                                             288257-05-6
     288257-06-7 288257-07-8 288257-08-9D, linker derivs.
     288257-09-0D, linker derivs.
                                   288257-10-3D, linker derivs.
     288257-11-4D, linker derivs. 288257-12-5D, linker derivs.
    288257-13-6D, linker derivs. 288257-14-7D, linker derivs.
    288257-15-8D, linker derivs.
                                    288257-16-9D, linker derivs.
     288257-17-0D, linker derivs.
                                    288257-18-1
                                                  288257-19-2
     288257-20-5
                   288257-21-6
                                 288257-22-7
                                                             288257-24-9
                                               288257-23-8
        (as ubiquitination recognition element; controlling
```

protein levels in eucaryotic organisms using novel
compds. comprising a ubiquitination recognition element and a
protein binding element and use as drugs and pesticides)

60267-61-0, Ubiquitin 74812-49-0, E3 Ubiquitin ligase (controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element and use as drugs and pesticides)

288257-29-4

ΙT

ΙT

(fluorescein antibodies targeted degrdn. stimulation by; controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element and use as drugs and pesticides)

IT 288257-28-3

(glutathione S-transferase targeted degrdn. stimulation by; controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element and use as drugs and pesticides)

IT 288257-25-0

(lysozyme targeted degrdn. stimulation by; controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element and use as drugs and pesticides)

IT 288257-26-1 (streptavidin targeted degrdn. stimulation by; controlling

protein levels in eucaryotic organisms using novel
compds. comprising a ubiquitination recognition element and a
protein binding element and use as drugs and pesticides)

IT 50812-37-8, Glutathione S-transferase

(targeted degrdn. of; controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element and use as drugs and pesticides)

IT 9001-63-2, Lysozyme

(targeted ubiquitination and degrdn. of; controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element and use as drugs and pesticides)

IT 9013-20-1, Streptavidin

(targeted ubiquitination of; controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element and use as drugs and pesticides)

IT 288387-73-5

(unclaimed protein sequence; controlling protein levels in eucaryotic organisms using novel

compds. comprising a ubiquitination recognition element and a protein binding element)

```
ΙT
    124676-51-3
                  124676-52-4
                                124676-53-5
                                              191606-36-7
                                                           223673-79-8
    246863-05-8
                  248909-28-6
                                248909-79-7
                                              248909-90-2
                                                           250255-96-0
    252032-31-8
                  268741-28-2
                                288315-45-7
                                              288315-49-1
                                                           288315-54-8
    288315-59-3
                  288315-61-7
                                288315-63-9
                                              288315-65-1
                                                           288315-67-3
    288315-69-5
                  288315-71-9
                                288315-73-1
                                              288315-75-3
                                                           288315-77-5
    288315-79-7
                  288315-82-2
                                288315-85-5
                                              288315-87-7
                                                           288315-89-9
    288315-91-3
                  288315-93-5
                                288315-95-7
                                              288315-97-9
                                                           288315-99-1
    288316-01-8
                  288316-03-0
                                288316-05-2
                                              288316-07-4
                                                           288316-10-9
                  288316-14-3
    288316-12-1
                                288316-16-5
                                              288387-74-6
```

(unclaimed sequence; controlling **protein** levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a **protein** binding element)

- L99 ANSWER 19 OF 28 HCA COPYRIGHT 2004 ACS on STN
- 131:141745 Energy transfer dyes as labels in biological systems. Flick, Parke (Amersham Pharmacia Biotech, Inc., USA). PCT Int. Appl. WO 9939203 A1 19990805, 31 pp. DESIGNATED STATES: W: AU, CA, JP; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US2105 19990202. PRIORITY: US 1998-18111 19980203.
- AB A novel class of energy transfer dyes, their prepn., and their use as labels in biol. systems is disclosed. The dyes are preferably in the form of cassettes which enable their attachment to a variety of biol. materials. The dyes and the reagents that can be made from them offer a wide variety of fluorescent labels with large Stokes' shifts enabling their use in a variety of fluorescence applications over a wide range of the visible spectrum. Prepn. of FAM-Cysteine-linker-ROX energy transfer dye from L-cysteine, 5-iodoacetamidofluorescein, trifluoroacetyl-protected NHS ester of 6-aminocaproic acid and 5'-ROX-NHS ester is described. With excitation at 488 nm, a strong peak was obsd. at 603 nm, characteristic of the ROX emission and indicating excellent energy transfer.
- IT 52-90-4, L-Cysteine, reactions

(in prepn. of energy transfer dye; energy transfer dyes as labels in biol. systems)

- RN 52-90-4 HCA
- CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 235749-12-9P

(in prepn. of energy transfer dye; energy transfer dyes as labels in biol. systems)

RN 235749-12-9 HCA

CN L-Cysteine, S-[2-[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)amino]-2-oxoethyl]-N-[1-oxo-6-[(trifluoroacetyl)amino]hexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IC ICM G01N033-533

ICS C07D311-82; C07D311-88; C07K016-00; C12N009-96; G01N033-52; G01N033-533; G01N033-545; G01N033-548; G01N033-552; G01N033-554

CC 9-14 (Biochemical Methods)

Section cross-reference(s): 41

IT Antibodies

Enzymes, uses

Lipids, uses

Nucleic acids

Peptides, uses

Proteins, specific or class

(conjugates, with dyes; energy transfer dyes as labels in biol. systems)

IT Antibodies

Antigens

Carbohydrates, reactions

DNA

Lipids, reactions
Nucleotides, reactions
Peptides, reactions

Proteins, general, reactions

RNA

(fluorescent labeling of; energy transfer dyes as labels in biol. systems)

IT **52-90-4**, L-Cysteine, reactions 63368-54-7,

5-Iodoacetamidofluorescein 117032-51-6 209734-74-7 (in prepn. of energy transfer dye; energy transfer dyes as labels in biol. systems)

IT 235749-11-8P 235749-12-9P

(in prepn. of energy transfer dye; energy transfer dyes as labels in biol. systems)

- L99 ANSWER 20 OF 28 HCA COPYRIGHT 2004 ACS on STN
- 131:29566 Devices and methods for detecting target molecules in biological samples. Muir, Andrew R.; Boles, Truett C.; Adams, Christopher P. (Mosaic Technologies, USA). PCT Int. Appl. WO 9926724 A2 19990603, 124 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US24918 19981125. PRIORITY: US 1997-66508 19971125.
- AB Devices and methods for detecting the presence, or absence of the presence, of at least one target mol. employing a receptacle housing a reaction chamber comprised of at least one compartment contg. suitable reagents for the detection of the target mol. are disclosed. The device can be used in particular for screening donated blood or other biol. fluids for the presence of contaminants. Preferably, the device comprises two or more breakable compartments sepd. by breakable barriers, and is assocd. with a collection system such as a blood bag. Probes and assays for detection of eubacterial contamination in platelet conc. are described.
- IT 518-44-5, Fluorescin

(donor probe labeled with, for detection of eubacterial 16S rRNA in platelet conc.; devices and methods for detecting target mols. in biol. samples)

RN 518-44-5 HCA

CN Benzoic acid, 2-(3,6-dihydroxy-9H-xanthen-9-yl)- (9CI) (CA INDEX NAME)

IC ICM B01L003-00

ICS G01N033-49; C12Q001-68; A61M001-02

CC 9-1 (Biochemical Methods)

Section cross-reference(s): 3, 10, 63

IT Chromophores

Fluorescent substances

Luminescent substances

Radioactive substances

(as **probe** label; devices and methods for detecting target mols. in biol. samples)

IT DNA

Nucleic acids

Peptides, analysis

Polynucleotides

Proteins, general, analysis

RNA

(as target; devices and methods for detecting target mols. in biol. samples)

IT Antibodies

(labeled, compartment contg., for detecting proteins; devices and methods for detecting target mols. in biol. samples)

IT 518-44-5, Fluorescin

(donor probe labeled with, for detection of eubacterial 16S rRNA in platelet conc.; devices and methods for detecting target mols. in biol. samples)

L99 ANSWER 21 OF 28 HCA COPYRIGHT 2004 ACS on STN

128:190109 A Homobifunctional Rhodamine for Labeling Proteins with Defined Orientations of a Fluorophore. Corrie, John E. T.; Craik, James S.; Munasinghe, V. Ranjit N. (National Institute for Medical Research, London, NW7 1AA, UK). Bioconjugate Chemistry, 9(2), 160-167 (English) 1998. CODEN: BCCHES. ISSN: 1043-1802. Publisher: American Chemical Society.

AB The synthesis and characterization of a bifunctional rhodamine dye bearing 2-(iodoacetamido)ethyl substituents on the 3'- and 6'-nitrogen atoms is described. Aspects of the conversion of chloroacetamides to iodoacetamides are discussed, including a

remarkably mild dehalogenation of an arom. haloacetamide in the presence of NaI and camphorsulfonic acid. The bifunctional rhodamine was designed for 2-site, 1:1 labeling of proteins that contain 2 suitably disposed cysteine residues and is intended to constrain the orientation of the rhodamine absorption and emission dipoles in a predictable relationship to the protein structure.

IT 203580-70-5P

(prepn. of homobifunctional rhodamine for labeling proteins)

RN 203580-70-5 HCA

CN Acetamide, N,N'-[(3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthene]-3',6'-diyl)bis[(methylimino)-2,1-ethanediyl]]bis[2-iodo-(9CI) (CA INDEX NAME)

IT 203580-79-4P

(prepn. of homobifunctional rhodamine for labeling proteins)

RN 203580-79-4 HCA

CN Acetamide, N,N'-[(3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthene]-3',6'-diyl)bis[(methylimino)-2,1-ethanediyl]]bis[2-chloro-(9CI) (CA INDEX NAME)

CC

9-14 (Biochemical Methods)

```
Section cross-reference(s): 28, 41
     homobifunctional rhodamine labeling protein prepn
ST
ΙT
     Proteins, specific or class
         (mercapto-contg.; prepn. of homobifunctional rhodamine for
        labeling proteins)
ΙT
     Fluorescent substances
        (prepn. of homobifunctional rhodamine for labeling
        proteins)
ΙΤ
     Dehalogenation
       Proteins, general, reactions
        (prepn. of homobifunctional rhodamine for labeling
        proteins)
ΙT
     Myosins
        (regulatory light-chain; prepn. of homobifunctional rhodamine for
        labeling proteins)
ΙΤ
     203580-80-7
        (prepn. of homobifunctional rhodamine for labeling
        proteins)
ΙT
     203580-70-5P
        (prepn. of homobifunctional rhodamine for labeling
        proteins)
IΤ
     98-09-9, Benzenesulfonyl chloride
                                         105-36-2, Ethyl bromoacetate
     630-88-6
                7452-78-0 26226-72-2
        (prepn. of homobifunctional rhodamine for labeling
        proteins)
ΙT
     14318-66-2P
                   33905-43-0P
                                 116465-51-1P
                                                203580-72-7P
     203580-73-8P
                    203580-74-9P
                                   203580-75-0P
                                                  203580-76-1P
                    203580-78-3P 203580-79-4P
     203580-77-2P
        (prepn. of homobifunctional rhodamine for labeling
        proteins)
IT
     5338-44-3P
                  6080-04-2P
                               203580-69-2P
        (prepn. of homobifunctional rhodamine for labeling
        proteins)
L99
     ANSWER 22 OF 28 HCA COPYRIGHT 2004 ACS on STN
127:288298 Irreversible Activation of the Gonadotropin-Releasing Hormone
     Receptor by Photoaffinity Crosslinking: Localization of Attachment
     Site to Cys Residue in N-Terminal Segment. Davidson, James S.;
     Assefa, Daniel; Pawson, Adam; Davies, Peter; Hapgood, Janet; Becker,
     Inga; Flanagan, Colleen; Roeske, Roger; Millar, Robert (M.R.C.
     Regulatory Peptides Research Unit Department of Chemical Pathology,
     University of Cape Town Medical School, Observatory, 7925, S. Afr.).
     Biochemistry, 36(42), 12881-12889 (English) 1997. CODEN: BICHAW.
     ISSN: 0006-2960. Publisher: American Chemical Society.
AB
     Photoaffinity crosslinking with [azidobenzoyl-D-Lys6]GnRH leads to
```

irreversible activation of the gonadotropin-releasing hormone (GnRH)

receptor. In order to localize the crosslinking site, the disulfide bridge structure was initially probed by mutagenesis. A consistent pattern of changes in the ability of GnRH to stimulate signal transduction after Ser substitutions of extracellularly located Cys residues indicated that Cys14 in the N-terminal domain is connected to Cys200 in the second extracellular loop, while Cys196 in this loop is connected to the highly conserved Cys114 at the extracellular end of transmembrane helix 3.

Protein chem. anal. of radioactive

fragments of cross-linked GnRH receptor following deglycosylation and enzymic digest with endoproteinase Glu-C and trypsin before and after introduction or elimination of potential protease cleavage sites indicated that 125I[azidobenzoyl-D-Lys6]GnRH cross-links to a segment comprising residues 12-18 of the N-terminal domain. The existence of the Cysl14-Cysl96 bridge was directly confirmed as a labeled fragment, including that Cys114 was resolvable only under reducing conditions. The observation that the cross-linked N-terminal enzymic fragments had identical apparent size under non-reducing conditions shows that the crosslinking reaction disconnected the disulfide bridge between Cys14 and Cys200 and indicates that Cys14 is probably the residue involved in crosslinking of the ligand. It is concluded that covalent tethering of GnRH through a photoreactive side chain located at position 6 in the middle of the peptide leads to continued activation of the receptor presumably through covalent binding to Cys14 in the N-terminal domain of the receptor.

IT 52-90-4, L-Cysteine, biological studies

(LH-RH receptor residue 14; LH-RH receptor irreversible activation by photoaffinity crosslinking with attachment to cysteine residue 14)

RN 52-90-4 HCA

CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ST

CC 2-2 (Mammalian Hormones)

LHRH receptor photoaffinity crosslinking disulfide bridge

IT Disulfide group

Signal transduction, biological

(LH-RH receptor irreversible activation by photoaffinity crosslinking with attachment to **cysteine** residue 14)

IT Gonadotropin-releasing hormone receptor

(LH-RH receptor irreversible activation by photoaffinity crosslinking with attachment to **cysteine** residue 14)

IT Conformation

(loop, protein; LH-RH receptor irreversible activation by photoaffinity crosslinking with attachment to **cysteine** residue 14)

IT Crosslinking

(photochem.; LH-RH receptor irreversible activation by photoaffinity crosslinking with attachment to **cysteine** residue 14)

IT Helix (conformation)

(protein; LH-RH receptor irreversible activation by photoaffinity crosslinking with attachment to **cysteine** residue 14)

IT 78527-81-8

(LH-RH receptor irreversible activation by photoaffinity crosslinking with attachment to **cysteine** residue 14)

IT 9034-40-6, LH-RH

(LH-RH receptor irreversible activation by photoaffinity crosslinking with attachment to **cysteine** residue 14)

IT 197100-47-3

(LH-RH receptor irreversible activation by photoaffinity crosslinking with attachment to **cysteine** residue 14)

- IT 52-90-4, L-Cysteine, biological studies
 (LH-RH receptor residue 14; LH-RH receptor irreversible activation by photoaffinity crosslinking with attachment to cysteine residue 14)
- L99 ANSWER 23 OF 28 HCA COPYRIGHT 2004 ACS on STN
- 127:231138 Peptidylglycine .alpha.-hydroxylating monooxygenase: active site residues, disulfide linkages, and a two-domain model of the catalytic core. Kolhekar, Aparna S.; Keutmann, Henry T.; Mains, Richard E.; Quon, Andrew S. W.; Eipper, Betty A. (Johns Hopkins University School of Medicine, Baltimore, MD, 21205-2105, USA). Biochemistry, 36(36), 10901-10909 (English) 1997. CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.
- Peptidylglycine .alpha.-hydroxylating monooxygenase (PHM) is a copper, ascorbate, and mol. oxygen dependent enzyme that catalyzes the first step leading to the C-terminal amidation of glycine-extended peptides. The catalytic core of PHM (PHMcc), refined to residues 42-356 of the PHM protein, was expressed at high levels in CHO (DG44) (dhfr-) cells. PHMcc has 10 cysteine residues involved in 5 disulfide linkages. Endoprotease Lys-C digestion of purified PHMcc under nonreducing conditions cleaved the protein at Lys219, indicating that the protein consists of separable N- and C-terminal domains with internal disulfide

linkages, that are connected by an exposed linker region. Disulfide-linked peptides generated by sequential

CNBr and pepsin treatment of radiolabeled PHMcc were sepd. by reverse phase HPLC and identified by Edman degrdn. disulfide linkages occur in the N-terminal domain (Cys47-Cys186, Cys81-Cys126, and Cys114-Cys131), along with three of the His residues crit. to catalytic activity (His107, His108, and His172). Two disulfide linkages (Cys227-Cys334 and Cys293-Cys315) occur in the C-terminal domain, along with the remaining two essential His residues (His242, His244) and Met314, thought to be essential in binding one of the two nonequivalent copper atoms. Substitution of Tyr79 or Tyr318 with Phe increased the Km of PHM for its peptidylglycine substrate without affecting Replacement of Glu313 with Asp increased the Km 8-fold and decreased the kcat 7-fold, again identifying this region of the C-terminal domain as crit. to catalytic activity. Taking into account information on the copper ligands in PHM, we propose a two-domain model with a copper site in each domain that allows spatial proximity between previously described copper ligands and residues identified as catalytically important.

IT 52-90-4, L-Cysteine, biological studies

(peptidylglycine .alpha.-hydroxylating monooxygenase: active site residues, disulfide linkages, and two-domain model of catalytic core)

RN 52-90-4 HCA

CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

CC 7-5 (Enzymes)

ST peptidylglycine alpha hydroxylating monooxygenase active site; disulfide group peptidylglycine alpha hydroxylating monooxygenase; copper site peptidylglycine alpha hydroxylating monooxygenase

IT Enzyme functional sites

(active; peptidylglycine .alpha.-hydroxylating monooxygenase: active site residues, disulfide linkages, and two-domain model of catalytic core)

IT Enzyme functional sites

(metal-binding; peptidylglycine .alpha.-hydroxylating monooxygenase: active site residues, disulfide linkages, and two-domain model of catalytic core)

IT Disulfide group

(peptidylglycine .alpha.-hydroxylating monooxygenase: active site

residues, disulfide linkages, and two-domain model of catalytic core)

- IT Conformation
 - (protein; peptidylglycine .alpha.-hydroxylating monooxygenase: active site residues, **disulfide** linkages, and two-domain model of catalytic core)
- TT 7440-50-8, Copper, biological studies 15158-11-9, Copper 2+, biological studies (peptidylglycine .alpha.-hydroxylating monooxygenase: active site residues, disulfide linkages, and two-domain model of catalytic core)
- L99 ANSWER 24 OF 28 HCA COPYRIGHT 2004 ACS on STN
 126:340782 Analyses of disulfides present in the rubella virus
 El glycoprotein. Gros, Christof; Linder, Monica; Wengler, Gisela;
 Wengler, Gerd (Institut fur Virologie, Justus-Liebig-Universitat
 Giessen, Giessen, 35392, Germany). Virology, 230(2), 179-186
 (English) 1997. CODEN: VIRLAX. ISSN: 0042-6822. Publisher:
 Academic.
- The surface of Rubella virus contains the glycoproteins E1 and E2. AΒ The El protein induces neutralizing antibodies and has been implicated in the process of recognition of cellular receptors. gain information on the structural organization of the E1 protein we have analyzed the disulfide bonds present within this mol. The reactivity of the protein with radioactively labeled iodoacetic acid indicates that all 20 **cysteine** residues present in the ectodomain of the El protein are involved in disulfide formation. protein was purified by preparative SDS-PAGE under nonreducing conditions from virus particles grown in tissue culture in the presence of [35S] cysteine. The purified protein was digested with a no. of proteases followed by reversed phase high-performance liq. chromatog. (HPLC). [35S]cvsteine -contg. peptides were identified and characterized by N-terminal amino acid sequence detn. These analyses identified the following eight disulfide bridges: C(1)-C(2); C(3)-C(15); C(6)-C(7); C(9)-C(10); C(11)-C(12); C(13)-C(14); C(17)-C(18); and C(19)-C(20). The two **disulfide** bridges formed by the residues C(4), C(5), C(8), and C(16) have not been identified with certainty, but a likely organization can be derived. obtained are discussed in the context of a possible structural and

functional organization of the El protein. 10-1 (Microbial, Algal, and Fungal Biochemistry) CC Section cross-reference(s): 6 ST rubella virus El protein disulfide ITGlycoproteins, specific or class (E1; analyses of disulfides present in rubella virus E1 glycoprotein) ΙΤ Conformation Protein sequences Rubella virus (analyses of disulfides present in rubella virus E1 glycoprotein) ΙT Disulfides (analyses of disulfides present in rubella virus E1 glycoprotein) ΙT Bond (sulfur-sulfur; analyses of disulfides present in rubella virus El glycoprotein) 1,99 ANSWER 25 OF 28 HCA COPYRIGHT 2004 ACS on STN 124:254489 Analysis of disulfide-containing fragments of Na+,K+-ATPase. III. Amino acid sequence of cysteinyl peptides. Location of disulfide bonds of .alpha.-subunit. Gevondyan, N. M.; Gavril'eva, E. E.; Gevondyan, V. S.; Grinberg, A. V.; Modyanov, N. N. (Shemyakin Ovchinnikov Inst. Bioorg. Chem., Moscow, Russia). Biologicheskie Membrany, 12(1), 22-8 (Russian) 1995. CODEN: BIMEE9. ISSN: 0233-4755. Publisher: Nauka. AΒ For localization of S-S bonds in the pig kidney Na+,K+-ATPase .alpha.-subunit, cysteine-contg. peptides (V-1, VII-1, and VII-2) obtained in the previous study from the enzyme's tryptic digest were analyzed. Chem. modification of the cysteine-contg. peptides performed by cysteine residues involved successive alkylations with radioactive iodoacetic acid and with ABD-F in the absence and presence of a reducing agent, resp. Cysteinyl peptides were isolated by HPLC, their amino acid sequences were detd. and two disulfide bonds, Cys452-Cys456 and Cys511-Cys549, were localized by identification of fluorescent cysteine residues. CC 7-5 (Enzymes) disulfide bond sodium potassium ATPase sequence ST ITProtein sequences (anal. of disulfide-contg. fragments of Na+,K+-ATPase. III. Amino acid sequence of cysteinyl peptides. Location of disulfide bonds of .alpha.-subunit) ΙΤ Swine

(anal. of disulfide-contg. fragments of pig Na+,K+-ATPase. III. Amino acid sequence of cysteinyl peptides. Location of disulfide bonds of .alpha.-subunit)

IT Bond

(sulfur-sulfur, anal. of **disulfide**-contg. fragments of Na+,K+-ATPase. III. Amino acid sequence of cysteinyl **peptides**. Location of **disulfide** bonds of .alpha.-subunit)

IT 9000-83-3, ATPase

(.alpha. subunit, sodium-potassium-dependent; anal. of disulfide-contg. fragments of Na+, K+-ATPase. III. Amino acid sequence of cysteinyl peptides. Location of disulfide bonds of the .alpha.-subunit)

- L99 ANSWER 26 OF 28 HCA COPYRIGHT 2004 ACS on STN

 120:293590 Separation method with auxiliary ligand-binder pairs in immunological detection of multiple analytes. Abuknesha, Ramadan Arbi (GEC-Marconi Ltd., UK). PCT Int. Appl. WO 9403807 A1 19940217, 71 pp. DESIGNATED STATES: W: CA, JP, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1993-GB1627 19930802. PRIORITY: GB 1992-16450 19920803; GB 1992-16683 19920806; GB 1992-19743 19920918; GB 1992-20722 19921001; GB 1992-24898 19921127; GB 1992-24897 19921127.
- AΒ A sepn. method which finds application in immunol. detection, a method suitable for use in detection, a sensor, and a test kit are disclosed. The invention provides a sepn. method suitable for use in an immunol. method for the detection of >1 species, which includes the use of >1 auxiliary ligand-binder pairs, the auxiliary ligand of each of the plurality of auxiliary ligand-binder pairs being provided on a support material. The invention also provides a sepn. method which includes the use of a plurality of auxiliary ligand-binder pairs, an auxiliary ligand of one auxiliary ligand-binder pair being provided on a support material and a binder of another auxiliary ligand-binder pair, which pair comprises an auxiliary ligand-auxiliary binder pair, being provided on a support material. The invention is useful for detection of multiple 17.beta.-Estradiol, progesterone and L-thyroxine were selected as analytes to illustrate the use of >1 auxiliary ligand-auxiliary binder pairs in sepns. of multiple analytes for immunol. detection. The auxiliary ligands used were 7-hydroxy-4-methylcoumarin-3propionic acid, 2-(4-aminophenyl)-6methylthiazole hemiglutarate, and 2-phenyl-4-quinoline carboxylic acid; auxiliary binders were antibodies to these ligands.

IT 154821-26-8

(as auxiliary ligand, antibody as auxiliary binder to, in sepn. in multiple analyte immunol. detection)

RN 154821-26-8 HCA

CN Glycine, N-[N-(9H-xanthen-9-ylcarbonyl)glycyl]- (9CI) (CA INDEX NAME)

IT 9003-53-6, Polystyrene

(support material, auxiliary ligand immobilized on, in sepn. for multiple analyte immunol. detection)

RN 9003-53-6 HCA

CN Benzene, ethenyl-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 100-42-5 CMF C8 H8

 $H_2C = CH - Ph$

IC ICM G01N033-537

ICS G01N033-543; G01N033-58

CC 9-10 (Biochemical Methods)

IT Hormones

Proteins, analysis

Steroids, analysis

Thyroid hormones

Toxins

(detection of, immunochem., auxiliary ligand-binder pair in sepn. in)

parr in sepir. In)

IT 51-28-5, 2,4-Dinitrophenol, analysis 58-85-5, Biotin 71-63-6, Digitoxin 91-64-5, Coumarin 132-60-5, 2-Phenyl-4-quinoline carboxylic acid 2321-07-5, Fluorescein 14202-13-2, 3-Methyl-1-adamantane acetic acid 18209-43-3 18530-30-8 24327-08-0 53127-08-5, Cibacron Blue 60835-71-4, 4-Amino-benzo-15-crown-5 72088-94-9, Carboxyfluorescein 76079-45-3 81925-04-4 154821-25-7 154821-26-8 154821-27-9, 4-Hydroxy-7-trifluoromethyl-3-quinaldinecarboxylic acid (as auxiliary ligand, antibody as auxiliary binder to, in sepn. in multiple analyte immunol. detection)

IT 9003-53-6, Polystyrene

(support material, auxiliary ligand immobilized on, in sepn. for multiple analyte immunol. detection)

L99 ANSWER 27 OF 28 HCA COPYRIGHT 2004 ACS on STN

- 114:38439 Peptidylchloromethyl ketone substrates for the detection of catalytically active serine proteases byimmuno assay. Mann, Kenneth G.; Williams, Brady; Tracy, Russell P. (University of Vermont and State Agricultural College, USA). PCT Int. Appl. WO 9003577 A1 19900405, 55 pp. DESIGNATED STATES: W: JP; RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1989-US4192 19890926. PRIORITY: US 1988-252506 19880930.
- AB Substituted peptidyl-chloromethyl ketone derivs. are irreversible inhibitors of serine proteinases. The peptide (1-3) amino acids) gives the compd. specificity for the active site of a particular proteinase. Substitution with a reporting group (e.g. biotin, a fluorophore) allows these substrates to be used in immunoassays for catalytically active serine These reagents measure active sites rather proteinases. than cross-reacting material (e.g. zymogens) and are therefore particularly suitable for the detn. of serine proteinase activity of blood coagulation factors. Biotinyl-.epsilon.-aminocaproyl-D-phenylalanyl-L-prolyl-L-arginine chloromethyl ketone (BC-PPACK) was synthesized by std. chem. and coupled to tissue-type plasminogen activator (tPA) to give tPA-BCPPACK. This was bound to avidin coated microtier plates and the bound tPA measured by immunoassay using peroxidase-coupled antibody. The std. curve showed a lower limit of sensitivity of 2 ng tPA/mL with test samples of 500 ng tPA/mL accurately measured.

IT 121593-25-7 121606-84-6 130056-27-8 130075-50-2 130404-52-3

(active site-specific fluorescent reagent for serine proteinases, immunoassays in relation to)

RN 121593-25-7 HCA

CN Glycinamide, N-[2-[3,6-bis(ethylamino)xanthylium-9-yl]benzoyl]-L-.alpha.-glutamyl-N-[4-[(aminoiminomethyl)amino]-1- (chloroacetyl)butyl]-, chloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

● Cl-

RN 121606-84-6 HCA

CN Glycinamide, N-[[4-[3,6-bis(diethylamino)xanthylium-9-yl]-3-sulfophenyl]sulfonyl]-L-.alpha.-glutamyl-N-[4-[(aminoiminomethyl)amino]-1-(chloroacetyl)butyl]-, inner salt, (S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 130056-27-8 HCA

CN L-Prolinamide, N-[[3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-

[9H]xanthen]-5(or 6)-yl]carbonyl]-L-phenylalanyl-N-[4-[(aminoiminomethyl)amino]-1-(chloroacetyl)butyl]- (9CI) (CA INDEX NAME)

RN 130075-50-2 HCA

CN Glycinamide, N-[3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5(or 6)-yl]-L-.alpha.-glutamyl-N-[4-[(aminoiminomethyl)amino]-1-(chloroacetyl)butyl]-, (S)- (9CI) (CA INDEX NAME)

RN 130404-52-3 HCA

CN L-Prolinamide, N-[[4-[3,6-bis(diethylamino)xanthylium-9-yl]-3-sulfophenyl]sulfonyl]-L-phenylalanyl-N-[4-[(aminoiminomethyl)amino]-1-(chloroacetyl)butyl]-, inner salt, (S)- (9CI) (CA INDEX NAME)

IT 121593-21-3P 121596-24-5P

(prepn. of, as active site-specific fluorescent reagent for serine proteinases)

RN 121593-21-3 HCA

CN Glycinamide, N-[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-6-yl)carbonyl]-L-.alpha.-glutamyl-N-[4-[(aminoiminomethyl)amino]-1-(chloroacetyl)butyl]-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

• HCl

PAGE 1-B

__ OH

RN 121596-24-5 HCA

CN Glycinamide, N-[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)carbonyl]-L-.alpha.-glutamyl-N-[4-[(aminoiminomethyl)amino]-1-(chloroacetyl)butyl]-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

HC1

PAGE 1-B

```
__ OH
```

ICM G01N033-573

IC

```
ICS G01N033-532; G01N033-543; C12Q001-38
CC
     7-3 (Enzymes)
     Section cross-reference(s): 9, 13, 15
ST
     serine proteinase active site assay reagent
ΙT
     Immunochemical analysis
        (colorimetric active site-specific immunoassay, serine
        proteinases detd. using, active site-specific
        chloromethyl ketone derivs. in)
     Immunochemical analysis
ΙΤ
        (immunoassay, serine proteinase detn. using,
        active site-specific chloromethyl ketone derivs. in)
ΙT
     Peptides, compounds
        (tri-, chloromethyl ketone analogs, conjugates, with biotin,
```

active site-specific reagents for serine proteinases, immunoassays using, blood-coagulation factors in relation to) 121593-24-6 **121593-25-7** ΙT 69024-84-6 104302-68-3 121606-84-6 130056-27-8 130075-50-2 130325-67-6 130325-68-7 130356-92-2 130290-58-3 130404-52-3 (active site-specific fluorescent reagent for serine proteinases, immunoassays in relation to) 9001-90-5, Plasmin 9002-04-4, Blood coagulation factor IIa ΙΤ 9002-05-5, Blood coagulation factor Xa 9039-53-6, Urokinase 37259-58-8, Serine **proteinase** 37316-87-3, Blood coagulation factor IXa 42617-41-4, Blood-coagulation factor XIVa 65312-43-8, Blood coagulation factor VIIA (detn. of, active site-specific chloromethylketones for, immunoassays using) ΙΤ 121593-20-2P 130290-57-2P (prepn. and reactions of, in prepn. serine proteinase active site-specific peptidyl chloromethyl ketones) ΙT **121593-21-3P 121596-24-5P** 121606-83-5P (prepn. of, as active site-specific fluorescent reagent for serine proteinases) ΙΤ 130290-54-9P 130290-55-0P (prepn. of, as active site-specific reagent for detn. of serine proteinase) ΙΤ 121593-23-5P 130290-54**-**9P 130290-56-1P (prepn. of, as active site-specific reagent for serine proteinases) ΙT 56-40-6, Glycine, reactions 109-02-4 543-27-1 2130-96-3 27601-29-2 35013-72-0 41296-45-1 6066-82-6 68715-98-0 72040-63-2 72088-94-9 82188-90-7 130290-57-2 71372-26-4 130325-66-5 (reactions of, in prepn. serine proteinase active site-specific peptidyl chloromethyl ketones) L99 ANSWER 28 OF 28 HCA COPYRIGHT 2004 ACS on STN 64:69205 Original Reference No. 64:12999h,13000a Variations in amino acid sequence near the disulfide bridges of Bence-Jones proteins. Milstein, C. (Med. Res. Council Lab. Mol. Biol., Cambridge, UK). Nature (London, United Kingdom), 209(5021), 370-3 (English) 1966. CODEN: NATUAS. ISSN: 0028-0836. Disulfide bridges of type K Bence-Jones proteins were AB quant. reduced and alkylated with iodoacetate-14C. radioactive protein was digested with trypsin or chymotrypsin and then fractionated on Sephadex. In the 8 proteins tested, the only variation in the C-terminal stretch was at position 189 where valine or leucine is found. The cysteine (I) residue toward the N-terminus showed a stretch of 22 residues after the 1st half of the mol. A

similarity of the sequences around I was found at residue 86 and 23 in some proteins. The 2 variable I residues formed a disulfide bridge. Proteins BJ and Rad had a region of variation between positions 90 and 94 with the 5 residues preceding it being identical. The peptide with I in position 23 of Bence-Jones was not found in Rad but a different peptide around a I residue was found. Protein Ker showed aspartic acid in positions 90 and 91 and the corresponding residues in Bence-Jones and in Rad were glutamic acid and asparagine and glutamic acid and threonine, resp. The heterogeneity of the L-chains of .gamma.-globulin may be the result of the heterogeneity of restricted stretches of the polypeptide chain.

CC 56 (General Biochemistry)

IT Proteins

(Bence-Jones, amino acid sequences near disulfide bridges of)

IT Amino acids.

(in Bence-Jones protein **disulfide** bridge vicinity, sequences of)

IT Disulfide group

(in Bence-Jones proteins, amino acid sequences in vicinity of)

=> d 1101 1-28 cbib abs hitstr hitind

L101 ANSWER 1 OF 28 HCA COPYRIGHT 2004 ACS on STN 139:334822 Cloning, sequence and physical characterization of enolase from pathogenic bacteria and their use as antimicrobial targets. Edwards, Aled; Dharamsi, Akil; Vedadi, Masoud; Domagala, Megan; Nethery, Kathleen; Buzadzija, Kristina; Houston, Simon; Ng, Ivy; Vallee, Francois; Awrey, Donald; Beattie, Bryan (Affinium Pharmaceuticals, Inc., Can.). PCT Int. Appl. WO 2003087352 A2 20031023, 439 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-CA506 20030409. PRIORITY: US 2002-PV371132 20020409; US 2002-PV371365 20020410; US 2002-PV371911 20020411. AΒ The present invention relates to novel drug targets for pathogenic The nucleic acid and amino acid sequences are provided for enolases from Staphylococcus aureus, Helicobacter pylori, and Streptococcus pneumoniae. The invention also provides bioinformatic, biochem. and biophys. characteristics of those

polypeptides, in particular characterization by mass spectrometry, NMR spectrometry, and x-ray crystallog. 7782-39-0, Hydrogen-2, uses ΙT (NMR isotope; cloning, sequence and phys. characterization of enolase from pathogenic bacteria and their use as antimicrobial targets) 7782-39-0 RNHCA CNDeuterium (7CI, 8CI, 9CI) (CA INDEX NAME) D— D ΙT 666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3, Methanol-d4 865-49-6, Chloroform-d 1076-43-3, Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9 2037-26-5 2206-26-0, Acetonitrile-d3 2206-27-1 2679-89-2 4472-41-7 7291-22-7, Pyridine-d5 7789-20-0 , Heavy water 17222-37-6 (deuterium lock solvent; cloning, sequence and phys. characterization of enolase from pathogenic bacteria and their use as antimicrobial targets) RN 666-52-4 HCA CN 2-Propanone-1,1,1,3,3,3-d6 (9CI) (CA INDEX NAME) D3C-C-CD3 RN811-98-3 HCA Methanol-d4 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME) CN D3C-0-D RN 865-49-6 HCA CN Methane-d, trichloro- (9CI) (CA INDEX NAME) D C1-C-C1C1

RN

1076-43-3 HCA

CN Benzene-d6 (8CI, 9CI) (CA INDEX NAME)

$$\begin{array}{c} D \\ D \\ D \end{array}$$

RN 1516-08-1 HCA

CN Ethanol-d6 (9CI) (CA INDEX NAME)

D3C-CD2-O-D

RN 1665-00-5 HCA

CN Methane-d2, dichloro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 1693-74-9 HCA

CN Furan-d4, tetrahydro-d4- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$$D \longrightarrow D$$

RN 2037-26-5 HCA

CN Benzene-d5, methyl-d3- (9CI) (CA INDEX NAME)

RN 2206-26-0 HCA

CN Acetonitrile-d3 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 2206-27-1 HCA

CN Methane-d3, sulfinylbis- (9CI) (CA INDEX NAME)

RN 2679-89-2 HCA

CN Ethane-d5, 2,2'-oxybis- (9CI) (CA INDEX NAME)

RN 4472-41-7 HCA

CN Formamide-1-d, N,N-di(methyl-d3)- (7CI, 8CI, 9CI) (CA INDEX NAME)

RN 7291-22-7 HCA

CN Pyridine-d5 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 17222-37-6 HCA

CN Methane-d3, oxybis- (9CI) (CA INDEX NAME)

D3C-0-CD3

IC ICM C12N009-00

CC 7-2 (Enzymes)

Section cross-reference(s): 1, 3, 10, 75

IT Antibacterial agents

Conformation

Cryoprotectants

Crystal growth

DNA sequences

Drug targets

Epitopes

Helicobacter pylori

Mass spectrometry

Molecular cloning

NMR spectroscopy

Pathogenic bacteria

Protein sequences

Staphylococcus aureus

Streptococcus pneumoniae

X-ray diffractometry

(cloning, sequence and phys. characterization of enolase from pathogenic bacteria and their use as antimicrobial targets)

IT Polyoxyalkylenes, uses

(low-mol.-wt., cryoprotectant; cloning, sequence and phys. characterization of enolase from pathogenic bacteria and their use as antimicrobial targets)

IT Gel electrophoresis

(protein purity detn.; cloning, sequence and

phys. characterization of enolase from pathogenic bacteria and their use as antimicrobial targets)

IT 1333-74-0, Hydrogen, uses 7440-23-5, Sodium-23, uses 7723-14-0, Phosphorus-31, uses 7727-37-9, Nitrogen-14, uses **7782-39-0**, Hydrogen-2, uses 7782-41-4, Fluorine-19, uses 10028-17-8, Hydrogen-3, uses 14390-96-6, Nitrogen-15, uses 14762-74-4, Carbon-13, uses

(NMR isotope; cloning, sequence and phys. characterization of enolase from pathogenic bacteria and their use as antimicrobial targets)

11 110-82-7, Cyclohexane, uses 666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3, Methanol-d4 865-49-6, Chloroform-d 1076-43-3, Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9 2037-26-5 2206-26-0, Acetonitrile-d3 2206-27-1

2679-89-2 4472-41-7 7291-22-7,

Pyridine-d5 7789-20-0, Heavy water 17222-37-6

(deuterium lock solvent; cloning, sequence and phys. characterization of enolase from pathogenic bacteria and their use as antimicrobial targets)

IT 25322-68-3, **PEG**

(low-mol.-wt., cryoprotectant; cloning, sequence and phys. characterization of enolase from pathogenic bacteria and their use as antimicrobial targets)

IT 59-67-6D, Nicotinic acid, derivs. 621-82-9D, Cinnamic acid, derivs.

(mass spectrometry matrix; cloning, sequence and phys. characterization of enolase from pathogenic bacteria and their use as antimicrobial targets)

L101 ANSWER 2 OF 28 HCA COPYRIGHT 2004 ACS on STN 139:319353 Cloning and physical characterization of microbial polypeptides involved in nucleotide transport and metabolism and their use as antimicrobial targets. Edwards, Aled; Dharamsi, Akil; Vedadi, Masoud; Domagala, Megan; Mansoury, Kamran; Houston, Simon; Awrey, Donald; Beattie, Bryan; Kanagarajah, Dhushy; Vallee, Francois; Virag, Cristina; Buzadzija, Kristina; Mcdonald, Merry-Lynn; Tai, Matthew; Pinder, Benjamin; Alam, Muhammad Zahoor; Ouyang, Hui; Richards, Dawn; Canadien, Veronica; Thalakada, Rosanne; Nethery, Kathleen (Affinium Pharmaceuticals, Inc., Can.). PCT Int. Appl. WO 2003087354 A2 20031023, 392 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE,

IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-CA485 20030408. PRIORITY: US 2002-PV371067 20020409; US 2002-PV386548 20020605; US 2002-PV386869 20020606; US 2002-PV386826 20020606; US 2002-PV424380 20021106; US 2002-PV425086 20021108; US 2002-PV436288 20021224; US 2002-PV436243 20021224; US 2002-PV436567 20021226; US 2002-PV436566 20021226; US 2002-PV436708 20021227; US 2002-PV437038 20021230; US 2002-PV436971 20021230; US 2002-PV437141 20021230; US 2002-PV436947 20021230; US 2002-PV437638 20021231; US 2002-PV437620 20021231.

The present invention relates to polypeptide targets for pathogenic bacteria. Reliable, high throughput methods are developed to identify, express, and purify a no. of antimicrobial targets from Staphylococcus aureus, Escherichia coli, Streptococcus pneumoniae, Enterococcus faecalis, Haemophilus influenzae, and Pseudomonas aeruginosa. The nucleic acid and amino acid sequences are provided for dUTPase, guanylate kinase, adenine phosphoribosyltransferase, thymidylate synthase, uridylate kinase, ribose phosphate pyrophosphokinase, and cytidine/deoxycytidylate deaminase family protein. The invention also provides bioinformatic, biochem. and biophys. characteristics of those polypeptides, in particular characterization by mass spectrometry, NMR spectrometry, and x-ray crystallog.

IT 7782-39-0, Hydrogen-2, uses

(NMR isotope; cloning and phys. characterization of microbial polypeptides involved in nucleotide transport and metab. and their use as antimicrobial targets)

RN 7782-39-0 HCA

CN Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME)

D-- D

RN

IT 666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3, Methanol-d4 865-49-6, Chloroform-d 917-96-4, Methyl-d3 isocyanide 1076-43-3, Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9, Tetrahydrofuran-d8 1735-17-7, Cyclohexane-d12 2037-26-5 2206-27-1, Dimethyl sulfoxide-d6 2679-89-2, Diethyl-d10 ether 4472-41-7, N,N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Deuterium oxide 17222-37-6, Dimethyl-d6 ether

(deuterium lock solvent for NMR spectroscopy; cloning and phys. characterization of microbial polypeptides involved in nucleotide transport and metab. and their use as antimicrobial targets)

666-52-4 HCA

CN 2-Propanone-1,1,1,3,3,3-d6 (9CI) (CA INDEX NAME)

D₃C- C- CD₃

RN 811-98-3 HCA

CN Methanol-d4 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

D3C-O-D

RN 865-49-6 HCA

CN Methane-d, trichloro- (9CI) (CA INDEX NAME)

C1-C-C1

RN 917-96-4 HCA

CN Methane-d3, isocyano- (9CI) (CA INDEX NAME)

 $D3C-N \stackrel{+}{=} C^-$

RN 1076-43-3 HCA

CN Benzene-d6 (8CI, 9CI) (CA INDEX NAME)

 $\begin{array}{c} D \\ D \\ D \\ \end{array}$

RN 1516-08-1 HCA

CN Ethanol-d6 (9CI) (CA INDEX NAME)

D3C-CD2-O-D

RN 1665-00-5 HCA CN Methane-d2, dichloro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 1693-74-9 HCA CN Furan-d4, tetrahydro-d4- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$$D \longrightarrow D$$

RN 1735-17-7 HCA CN Cyclohexane-d12 (6CI, 8CI, 9CI) (CA INDEX NAME)

RN 2037-26-5 HCA CN Benzene-d5, methyl-d3+ (9CI) (CA INDEX NAME)

RN 2206-27-1 HCA CN Methane-d3, sulfinylbis- (9CI) (CA INDEX NAME)

RN 2679-89-2 HCA

CN Ethane-d5, 2,2'-oxybis- (9CI) (CA INDEX NAME)

 $D_3C-CD_2-O-CD_2-CD_3$

RN 4472-41-7 HCA

CN Formamide-1-d, N, N-di(methyl-d3) - (7CI, 8CI, 9CI) (CA INDEX NAME)

RN 7291-22-7 HCA

CN Pyridine-d5 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$$\begin{array}{c} D \\ \end{array}$$

RN 7789-20-0 HCA

CN Water-d2 (9CI) (CA INDEX NAME)

D- O- D

RN 17222-37-6 HCA

CN Methane-d3, oxybis- (9CI) (CA INDEX NAME)

D3C-0-CD3

IC ICM C12N009-14

ICS C12N015-55

CC 7-2 (Enzymes)

Section cross-reference(s): 1, 3, 6, 10

ST essential protein pathogenic bacteria therapeutic target; sequence

ΙT

ΙT

ΙΤ

IΤ

ΙT

ΙT

```
essential protein gene pathogenic bacteria; mass
spectrometry essential protein pathogenic
bacteria; NMR spectrometry essential protein
pathogenic bacteria; xray crystallog essential protein pathogenic
bacteria; cloning essential protein pathogenic bacteria
Molecular chaperones
   (DnaK, protein-protein interactions of; cloning and phys.
   characterization of microbial polypeptides involved in
   nucleotide transport and metab. and their use as antimicrobial
   targets)
Molecular chaperones
   (GroEL, protein-protein interactions of; cloning and phys.
   characterization of microbial polypeptides involved in
   nucleotide transport and metab. and their use as antimicrobial
   targets)
Antibacterial agents
Cryoprotectants
Crystallization
DNA sequences
Drug design
Drug screening
Drug targets
Enterococcus faecalis
Epitopes
Escherichia coli
Haemophilus influenzae
  Mass spectrometry
Molecular cloning
NMR spectroscopy
Pathogenic bacteria
Protein sequences
Pseudomonas aeruginosa
Staphylococcus aureus
Streptococcus pneumoniae
   (cloning and phys. characterization of microbial
   polypeptides involved in nucleotide transport and metab.
   and their use as antimicrobial targets)
Hydrocarbon oils
  Polyoxyalkylenes, uses
   (cryoprotectant; cloning and phys. characterization of microbial
   polypeptides involved in nucleotide transport and metab.
   and their use as antimicrobial targets)
Solvents
   (deuterium lock, for NMR spectroscopy; cloning and
   phys. characterization of microbial polypeptides
   involved in nucleotide transport and metab. and their use as
   antimicrobial targets)
Fusion proteins (chimeric proteins)
```

(for improved soly. or stability; cloning and phys. characterization of microbial **polypeptides** involved in nucleotide transport and metab. and their use as antimicrobial targets)

IT Elements

(heavy, for mass spectrometry; cloning and phys. characterization of microbial polypeptides involved in nucleotide transport and metab. and their use as antimicrobial targets)

IT Proteins

(in nucleotide transport and metab.; cloning and phys. characterization of microbial **polypeptides** involved in nucleotide transport and metab. and their use as antimicrobial targets)

IT Molecular association

(protein-protein; cloning and phys. characterization of microbial polypeptides involved in nucleotide transport and metab. and their use as antimicrobial targets)

Nucleotides, biological studies
(proteins involved in transport and metab. of; cloning and phys.
characterization of microbial polypeptides involved in
nucleotide transport and metab. and their use as antimicrobial
targets)

IT Crystallography

ΙT

(x-ray; cloning and phys. characterization of microbial polypeptides involved in nucleotide transport and metab. and their use as antimicrobial targets)

7440-23-5, Sodium-23, uses 7723-14-0, Phosphorus-31, uses 7727-37-9, Nitrogen-14, uses **7782-39-0**, Hydrogen-2, uses 7782-41-4, Fluorine-19, uses 10028-17-8, Hydrogen-3, uses 12184-88-2, Hydride 14390-96-6, Nitrogen-15, uses 14762-74-4, Carbon-13, uses

(NMR isotope; cloning and phys. characterization of microbial polypeptides involved in nucleotide transport and metab. and their use as antimicrobial targets)

1T 612552-95-1P 612552-98-4P 612553-00-1P 612553-02-3P 612553-04-5P 612553-06-7P 612553-09-0P 612553-11-4P 612553-13-6P 612553-15-8P 612553-17-0P 612553-19-2P 612553-21-6P 612553-23-8P 612553-30-7P 612553-32-9P 612553-34-1P 612553-36-3P 612553-39-6P 612553-41-0P

(amino acid sequence; cloning and phys. characterization of microbial polypeptides involved in nucleotide transport and metab. and their use as antimicrobial targets)

9015-83-2P, Ribose phosphate pyrophosphokinase 9026-59-9P, Guanylate kinase 9027-80-9P, Adenine phosphoribosyltransferase 9031-61-2P, Thymidylate synthase 9036-23-1P, Uridylate kinase 37289-34-2P

(cloning and phys. characterization of microbial polypeptides involved in nucleotide transport and metab. and their use as antimicrobial targets) 56-81-5, Glycerol, uses 64-18-6, Formic acid, uses 67-63-0, ΙT Isopropanol, uses 77-92-9, Citric acid, uses 107-21-1, Ethylene 5683-44-3, 3-Methyl-2,4-pentanediol 25322-68-3, glycol, uses Polyethylene glycol (cryoprotectant; cloning and phys. characterization of microbial polypeptides involved in nucleotide transport and metab. and their use as antimicrobial targets) 666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3, IT Methanol-d4 865-49-6, Chloroform-d 917-96-4, Methyl-d3 isocyanide 1076-43-3, Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9 , Tetrahydrofuran-d8 1735-17-7, Cyclohexane-d12 2037-26-5 2206-27-1, Dimethyl sulfoxide-d6 2679-89-2, Diethyl-d10 ether 4472-41-7, N, N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Deuterium oxide 17222-37-6, Dimethyl-d6 ether (deuterium lock solvent for NMR spectroscopy; cloning and phys. characterization of microbial polypeptides involved in nucleotide transport and metab. and their use as antimicrobial targets) 9025-06-3P, Cytidine deaminase 9026-92-0P, Deoxycytidylate ΙΤ deaminase (family member; cloning and phys. characterization of microbial polypeptides involved in nucleotide transport and metab. and their use as antimicrobial targets) 7429-91-6, Dysprosium, uses 7439-88-5, Iridium, uses 7439-90-9, ΙT Krypton, uses 7439-91-0, Lanthanum, uses 7439-92-1, Lead, uses 7439-94-3, Lutetium, uses 7439-97-6, Mercury, uses 7439-98-7, Molybdenum, uses 7440-00-8, Neodymium, uses 7440-04-2, Osmium, 7440-05-3, Palladium, uses 7440-06-4, Platinum, uses 7440-10-0, Praseodymium, uses 7440-15-5, Rhenium, uses 7440-16-6, Rhodium, uses 7440-18-8, Ruthenium, uses 7440-19-9, 7440-22-4, Silver, uses 7440-24-6, Strontium, Samarium, uses 7440-25-7, Tantalum, uses 7440-27-9, Terbium, uses uses 7440-28-0, Thallium, uses 7440-29-1, Thorium, uses 7440-30-4, 7440-31-5, Tin, uses 7440-33-7, Tungsten, uses Thulium, uses 7440-39-3, Barium, uses 7440-43-9, Cadmium, uses 7440-45-1, 7440-48-4, Cobalt, uses 7440-52-0, Erbium, uses Cerium, uses 7440-53-1, Europium, uses 7440-54-2, Gadolinium, uses 7440-57-5, Gold, uses 7440-60-0, Holmium, uses 7440-61-1, Uranium, uses 7440-63-3, Xenon, uses 7440-64-4, Ytterbium, uses 7553-56-2,

Iodine, uses 7726-95-6, Bromine, uses 7782-49-2, Selenium, uses

and phys. characterization of microbial polypeptides

(heavy atom for mass spectrometry; cloning

involved in nucleotide transport and metab. and their use as antimicrobial targets) ΙT 59-67-6D, Nicotinic acid, derivs. 621-82-9D, Cinnamic acid, derivs. (mass spectrometry of; cloning and phys. characterization of microbial polypeptides involved in nucleotide transport and metab. and their use as antimicrobial targets) ΙT 612552-94-0, DNA (Streptococcus pneumoniae gene dut) 612552-96-2. DNA (Streptococcus pneumoniae gene dut) 612552-97-3, DNA 612552-99-5, DNA (Pseudomonas (Staphylococcus aureus gene qmk) 612553-01-2, DNA (Pseudomonas aeruginosa gene aeruginosa gene APT) 612553-03-4, DNA (Pseudomonas aeruginosa gene PRSA) 612553-05-6, DNA (Pseudomonas aeruginosa gene gmk) 612553-07-8, DNA (Pseudomonas aeruginosa gene gmk) 612553-08-9, DNA 612553-10-3, DNA (Enterococcus (Enterococcus faecalis gene thyA) 612553-12-5, DNA (Enterococcus faecalis gene faecalis gene thyA) 612553-14-7, DNA (Escherichia coli gene gmk) PYRH) 612553-16-9, DNA (Enterococcus faecalis gene APT) 612553-18-1, DNA 612553-20-5, DNA (Enterococcus (Enterococcus faecalis gene APT) faecalis gene gmk) 612553-22-7, DNA (Enterococcus faecalis gene 612553-24-9, DNA (Enterococcus faecalis gene PRSA) 612553-25-0, DNA (Haemophilus influenzae gene KTHY) 612553-27-2, DNA (Haemophilus influenzae gene KTHY) 612553-29-4, DNA (Haemophilus influenzae gene APT) 612553-31-8, DNA (Haemophilus 612553-33-0, DNA (Haemophilus influenzae gene influenzae gene gmk) 612553-35-2, DNA (Pseudomonas aeruginosa gene KTHY) 612553-37-4, DNA (Pseudomonas aeruginosa gene KTHY) 612553-38-5, DNA (Streptococcus pneumoniae gene KTHY) 612553-40-9, DNA (Streptococcus pneumoniae gene YHFC) 612553-42-1, DNA (Streptococcus pneumoniae gene YHFC) (nucleotide sequence; cloning and phys. characterization of microbial polypeptides involved in nucleotide transport and metab. and their use as antimicrobial targets) ΙT 3211-76-5, Selenomethionine (protein label for mass spectrometry; cloning and phys. characterization of microbial polypeptides involved in nucleotide transport and metab. and their use as antimicrobial targets) 612572-78-8 612572-79-9 612572-80-2 612572-81-3 612572-82-4 ΙT 612572-84-6 612572-83-5 612572-85-7 612572-86-8 612572-87-9 612572-91-5 612572-92-6 612572-93-7 612572-88-0 612572-89-1 612572-97-1 612572-94-8 612572-95-9 612572-96-0 612572-98-2 612573-00-9 612573-01-0 612573-02-1 612573-03-2 612573-04-3 612573-05-4 612573-06-5 612573-07-6 612573-08-7 612573-09-8 612573-11-2 612573-12-3 612573-13-4 612573-10-1

(unclaimed nucleotide sequence; cloning and phys.

characterization of microbial polypeptides involved in

nucleotide transport and metab. and their use as antimicrobial targets) ΙT 612572-90-4 612572-99-3 (unclaimed protein sequence; cloning and phys. characterization of microbial polypeptides involved in nucleotide transport and metab. and their use as antimicrobial targets) ΙT 612512-63-7 612512-64-8 612512-65-9 612512-66-0 612512-67-1 612512-68-2 612512-69-3 612512-70-6 612512-71-7 612512-72-8 612512-73-9 612512-74-0 612512-75-1 612512-76-2 612512-77-3 612512-78-4 612512-79-5 612512-80-8 612512-81-9 612512-82-0 612512-83-1 612512-84-2 612512-85-3 612512-86-4 612512-87-5 612512-88-6 612512-89-7 612512-90-0 612512-91-1 612512-92-2 612512-93-3 612512-94-4 612512-95-5 612512-96-6 612512-97-7 612512-98-8 612512-99-9 612513-00-5 612513-01-6 612513-02-7 612513-03-8 612513-04-9 .612513-05-0 612513-06-1 612513-07-2 612513-10-7 612513-08-3 612513-09-4 (unclaimed sequence; cloning and phys. characterization of microbial polypeptides involved in nucleotide transport and metab. and their use as antimicrobial targets)

L101 ANSWER 3 OF 28 HCA COPYRIGHT 2004 ACS on STN 139:319352 Cloning and physical characterization of microbial polypeptides involved in membrane biogenesis and their use as antimicrobial targets. Edwards, Aled; Dharamsi, Akil; Vedadi, Masoud; Domagala, Megan; Houston, Simon; Awrey, Donald; Beattie, Bryan; Mansoury, Kamran; Ouyang, Hui; Vallee, Francois; Richards, Dawn; Nethery, Kathleen; Virag, Cristina; Buzadzija, Kristina; Pinder, Benjamin; Alam, Muhammad Zahoor; Tai, Matthew; Canadien, Veronica; Kanagarajah, Dhushy; Thalakada, Rosanne (Affinium Pharmaceuticals, Inc., Can.). PCT Int. Appl. WO 2003087353 A2 20031023, 407 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-CA481 20030408. PRIORITY: US 2002-PV370915 20020408; US 2002-PV370899 20020408; US 2002-PV371185 20020409; US 2002-PV371107 20020409; US 2002-PV385426 20020531; US 2002-PV386283 20020606; US 2002-PV400348 20020801; US 2002-PV424395 20021106; US 2002-PV425200 20021108; US 2002-PV436345 20021224; US 2002-PV436349 20021224; US 2002-PV436568 20021226; US 2002-PV436893 20021227; US 2002-PV436889 20021227; US 2002-PV436675 20021227; US 2002-PV436900 20021227; US 2002-PV436885 20021227; US 2002-PV436734 20021227; US 2002-PV437013 20021230.

AΒ The present invention relates to polypeptide targets for pathogenic bacteria. Reliable, high throughput methods are developed to identify, express, and purify a no. of antimicrobial targets from Staphylococcus aureus, Escherichia coli, Streptococcus pneumoniae, Enterococcus faecalis, Haemophilus influenzae, and Pseudomonas aeruginosa. The nucleic acid and amino acid sequences are provided for UDP-acetylglucosamine 1-carboxyvinyltransferase 1, CTP:CMP-3-deoxy-D-mannooctulosonate transferase, UDP-acetylmuramoylalanyl-D-glutamate-2,6-diaminopimelate ligase, D-alanine: D-alanine-adding enzyme, D-alanine: D-alanine ligase, UDP-acetylpyruvoylglucosamine reductase,, UDP-acetylglucosamine pyrophosphorylase, UDP-acetylmuramoylalanine-D-glutamate ligase, UDP-acetylmuramate: alanine ligase, and aspartate semialdehyde dehydrogenase. The invention also provides bioinformatic, biochem. and biophys. characteristics of those polypeptides, in particular characterization by mass spectrometry , NMR spectrometry, and x-ray crystallog. 7782-39-0, Hydrogen-2, uses IT(NMR isotope; cloning and phys. characterization of microbial polypeptides involved in membrane biogenesis and their use as antimicrobial targets) RN7782-39-0 HCA Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME) CN D-- D 666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3, ΙT Methanol-d4 865-49-6, Chloroform-d 917-96-4, Methyl-d3 isocyanide 1076-43-3, Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9 , Tetrahydrofuran-d8 1735-17-7, Cyclohexane-d12 2037-26-5 2206-27-1, Dimethyl sulfoxide-d6 2679-89-2, Diethyl-d10 ether 4472-41-7, N, N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Deuterium oxide 17222-37-6, Dimethyl-d6 ether (deuterium lock solvent for NMR spectroscopy; cloning and phys. characterization of microbial polypeptides involved in membrane biogenesis and their use as antimicrobial targets) 666-52-4 RNHCA 2-Propanone-1, 1, 1, 3, 3, 3-d6 (9CI) (CA INDEX NAME) CN

RN 811-98-3 HCA

CN Methanol-d4 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

D3C-0-D

RN 865-49-6 HCA

CN Methane-d, trichloro- (9CI) (CA INDEX NAME)

RN 917-96-4 HCA

CN Methane-d3, isocyano- (9CI) (CA INDEX NAME)

RN 1076-43-3 HCA

CN Benzene-d6 (8CI, 9CI) (CA INDEX NAME)

$$\begin{array}{c|c} D & D \\ \hline D & D \\ \hline \end{array}$$

RN 1516-08-1 HCA

CN Ethanol-d6 (9CI) (CA INDEX NAME)

D3C-CD2-O-D

RN 1665-00-5 HCA

CN Methane-d2, dichloro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

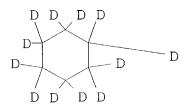
RN 1693-74-9 HCA

CN Furan-d4, tetrahydro-d4- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$$D \longrightarrow D \longrightarrow D$$

RN 1735-17-7 HCA

CN Cyclohexane-d12 (6CI, 8CI, 9CI) (CA INDEX NAME)



RN 2037-26-5 HCA

CN Benzene-d5, methyl-d3- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} D & CD3 \\ \hline D & D \\ \end{array}$$

RN 2206-27-1 HCA

CN Methane-d3, sulfinylbis- (9CI) (CA INDEX NAME)

RN 2679-89-2 HCA

CN Ethane-d5, 2,2'-oxybis- (9CI) (CA INDEX NAME)

D3C-CD2-O-CD2-CD3

RN 4472-41-7 HCA

CN Formamide-1-d, N, N-di(methyl-d3)- (7CI, 8CI, 9CI) (CA INDEX NAME)

RN 7291-22-7 HCA

CN Pyridine-d5 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$$\begin{array}{c} D \\ \end{array}$$

RN 7789-20-0 HCA

CN Water-d2 (9CI) (CA INDEX NAME)

D- O- D

RN 17222-37-6 HCA

CN Methane-d3, oxybis- (9CI) (CA INDEX NAME)

D3C- O- CD3

IC ICM C12N009-10

CC 7-2 (Enzymes)

Section cross-reference(s): 1, 3, 6, 10

ST essential protein pathogenic bacteria therapeutic target; sequence essential protein gene pathogenic bacteria; mass

ΙT

ΙT

IT

ΙT

ΙT

ΙT

ΙT

spectrometry essential protein pathogenic bacteria; NMR spectrometry essential protein pathogenic bacteria; xray crystallog essential protein pathogenic bacteria; cloning essential protein pathogenic bacteria Heat-shock proteins (HSP 70, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in membrane biogenesis and their use as antimicrobial targets) Ribosomal proteins (L2, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in membrane biogenesis and their use as antimicrobial targets) Enzymes, biological studies (RNA helicase, ATP-dependent, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in membrane biogenesis and their use as antimicrobial targets) Ribosomal proteins (S1, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in membrane biogenesis and their use as antimicrobial targets) Ribosomal proteins (S10, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in membrane biogenesis and their use as antimicrobial targets) Antibacterial agents Cryoprotectants Crystallization DNA sequences Drug design Drug screening Drug targets Enterococcus faecalis Epitopes Escherichia coli Haemophilus influenzae Mass spectrometry Molecular cloning NMR spectroscopy Pathogenic bacteria Protein sequences Pseudomonas aeruginosa Staphylococcus aureus Streptococcus pneumoniae (cloning and phys. characterization of microbial polypeptides involved in membrane biogenesis and their use as antimicrobial targets) Hydrocarbon oils

Polyoxyalkylenes, uses

(cryoprotectant; cloning and phys. characterization of microbial **polypeptides** involved in membrane biogenesis and their use as antimicrobial targets)

IT Solvents

(deuterium lock, for NMR spectroscopy; cloning and phys. characterization of microbial polypeptides involved in membrane biogenesis and their use as antimicrobial targets)

- IT Elements
 (heavy, for mass spectrometry; cloning and phys. characterization of microbial polypeptides involved in membrane biogenesis and their use as antimicrobial targets)
- IT Proteins
 (in membrane biogenesis; cloning and phys. characterization of microbial polypeptides involved in membrane biogenesis and their use as antimicrobial targets)

- IT Membrane, biological (proteins involved in biogenesis of; cloning and phys. characterization of microbial polypeptides involved in membrane biogenesis and their use as antimicrobial targets)
- TT 7440-23-5, Sodium-23, uses 7723-14-0, Phosphorus-31, uses 7727-37-9, Nitrogen-14, uses **7782-39-0**, Hydrogen-2, uses 7782-41-4, Fluorine-19, uses 10028-17-8, Hydrogen-3, uses 12184-88-2, Hydride 14390-96-6, Nitrogen-15, uses 14762-74-4, Carbon-13, uses

(NMR isotope; cloning and phys. characterization of microbial polypeptides involved in membrane biogenesis and their use as antimicrobial targets)

IT 612553-71-6P 612553-77-2P 612553-78-3P 612553-80-7P 612553-82-9P 612553-84-1P 612553-86-3P 612553-88-5P

ΙΤ

ΙT

ΙT

ΙT

```
612553-92-1P
               612553-90-9P
                              612553-91-0P
612553-89-6P
                                             612554-00-4P
                              612553-98-7P
               612553-96-5P
612553-94-3P
                              612554-06-0P
                                             612554-08-2P
               612554-04-8P
612554-02-6P
               612554-10-6P
                              612554-11-7P
                                             612554-12-8P
612554-09-3P
                                             612554-16-2P
                              612554-15-1P
               612554-14-0P
612554-13-9P
                              612554-20-8P
                                             612854-64-5P
               612554-18-4P
612554-17-3P
612854-66-7P
   (amino acid sequence; cloning and phys. characterization of
  microbial polypeptides involved in membrane biogenesis
   and their use as antimicrobial targets)
612553-73-8
              612553-75-0
   (amino acid sequence; cloning and phys. characterization of
  microbial polypeptides involved in membrane biogenesis
   and their use as antimicrobial targets)
9000-98-0P, Aspartate semialdehyde dehydrogenase
                                                   9023-06-7P,
UDP-acetylglucosamine pyrophosphorylase 9023-27-2P,
UDP-N-acetylglucosamine 1-carboxyvinyltransferase
                                                    9023-52-3P,
UDP-N-acetylmuramate:L-alanine ligase
                                       9023-59-0P,
UDP-N-acetylmuramoylalanine-D-glutamate ligase
                                                9023-63-6P,
                            9075-09-6P, UDP-N-acetylmuramyl-L-
D-Alanine: D-alanine ligase
alanyl-D-glutamate:2,6-diaminopimelate ligase
                                                37278-28-7P,
CTP:CMP-3-deoxy-mannooctulosonate cytidylyltransferase
39307-28-3P, UDP-acetylenolpyruvylglucosamine reductase
55354-36-4P, D-Alanyl-D-alanine-adding enzyme
   (cloning and phys. characterization of microbial
   polypeptides involved in membrane biogenesis and their
   use as antimicrobial targets)
                          64-18-6, Formic acid, uses
56-81-5, Glycerol, uses
                   77-92-9, Citric acid, uses 107-21-1, Ethylene
Isopropanol, uses
               5683-44-3, 3-Methyl-2, 4-pentanediol
                                                    25322-68-3,
glycol, uses
Polyethylene glycol
   (cryoprotectant; cloning and phys. characterization of microbial
   polypeptides involved in membrane biogenesis and their
   use as antimicrobial targets)
666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3,
Methanol-d4 865-49-6, Chloroform-d 917-96-4,
Methyl-d3 isocyanide 1076-43-3, Benzene-d6
1516-08-1, Ethanol-d6 1665-00-5 1693-74-9
, Tetrahydrofuran-d8 1735-17-7, Cyclohexane-d12
2037-26-5 2206-27-1, Dimethyl sulfoxide-d6
2679-89-2, Diethyl-d10 ether 4472-41-7,
N, N-Dimethylformamide-d7 7291-22-7, Pyridine-d5
7789-20-0, Deuterium oxide 17222-37-6,
Dimethyl-d6 ether
   (deuterium lock solvent for NMR spectroscopy; cloning
   and phys. characterization of microbial polypeptides
   involved in membrane biogenesis and their use as antimicrobial
   targets)
```

ΙT 7429-91-6, Dysprosium, uses 7439-88-5, Iridium, uses 7439-90-9, Krypton, uses 7439-91-0, Lanthanum, uses 7439-92-1, Lead, uses 7439-94-3, Lutetium, uses 7439-97-6, Mercury, uses 7439-98-7, Molybdenum, uses 7440-00-8, Neodymium, uses 7440-04-2, Osmium, 7440-05-3, Palladium, uses 7440-06-4, Platinum, uses 7440-10-0, Praseodymium, uses 7440-15-5, Rhenium, uses 7440-16-6, Rhodium, uses 7440-18-8, Ruthenium, uses Samarium, uses 7440-22-4, Silver, uses 7440-24-6, Strontium, 7440-25-7, Tantalum, uses 7440-27-9, Terbium, uses 7440-28-0, Thallium, uses 7440-29-1, Thorium, uses 7440-30-4. 7440-31-5, Tin, uses 7440-33-7, Tungsten, uses Thulium, uses 7440-39-3, Barium, uses 7440-43-9, Cadmium, uses 7440-45-1, 7440-48-4, Cobalt, uses 7440-52-0, Erbium, uses Cerium, uses 7440-53-1, Europium, uses 7440-54-2, Gadolinium, uses Gold, uses 7440-60-0, Holmium, uses 7440-61-1, Uranium, uses 7440-63-3, Xenon, uses 7440-64-4, Ytterbium, uses 7553-56-2, 7726-95-6, Bromine, uses 7782-49-2, Selenium, uses Iodine, uses (heavy atom for mass spectrometry; cloning and phys. characterization of microbial polypeptides involved in membrane biogenesis and their use as antimicrobial targets) 59-67-6D, Nicotinic acid, derivs. 621-82-9D, Cinnamic acid, ΙT

derivs. (mass spectrometry of; cloning and phys.

characterization of microbial polypeptides involved in membrane biogenesis and their use as antimicrobial targets) 612553-74-9P, DNA (Staphylococcus aureus gene murA) (nucleotide sequence; cloning and phys. characterization of

ΙT

ТТ

microbial polypeptides involved in membrane biogenesis and their use as antimicrobial targets)

612553-70-5, DNA (Pseudomonas aeruginosa gene murA) 612553-72-7, 612553-79-4, DNA DNA (Pseudomonas aeruginosa gene murA) (Escherichia coli gene kdsB) 612553-81-8, DNA (Escherichia coli 612553-83-0, DNA (Haemophilus pneumoniae gene kdsB) gene kdsB) 612553-85-2, DNA (Pseudomonas aeruginosa gene murE) 612553-87-4, DNA (Pseudomonas aeruginosa gene murE) 612553-93-2, DNA (Pseudomonas aeruginosa gene murF) 612553-95-4, DNA (Pseudomonas aeruginosa gene murF) 612553-97-6, DNA (Enterococcus faecalis gene 612553-99-8, DNA (Enterococcus faecalis gene ddlA) 612554-01-5, DNA (Pseudomonas aeruginosa gene murB) 612554-03-7, DNA (Pseudomonas aeruginosa gene murB) 612554-05-9, DNA (Haemophilus influenzae gene murB) 612554-07-1, DNA (Haemophilus influenzae gene murB) 612554-19-5, DNA (Haemophilus influenzae 612854-49-6, DNA (Streptococcus pneumoniae gene murA) 612854-50-9, DNA (Streptococcus pneumoniae gene murA) 612854-51-0, DNA (Haemophilus influenzae gene murE) 612854-52-1, DNA (Haemophilus influenzae gene murE) 612854-53-2, DNA (Staphylococcus aureus gene murF) 612854-54-3, DNA (Staphylococcus

```
aureus gene murF)
                    612854-55-4, DNA (Enterococcus faecalis gene
        612854-56-5, DNA (Enterococcus faecalis gene glmU)
612854-57-6, DNA (Haemophilus influenzae gene glmU)
                                                       612854-58-7.
DNA (Haemophilus influenzae gene glmU)
                                         612854-59-8, DNA
(Staphylococcus aureus gene glmU)
                                   612854-60-1, DNA (Staphylococcus
                    612854-61-2, DNA (Enterococcus faecalis gene
aureus gene glmU)
        612854-62-3, DNA (Enterococcus faecalis gene murD)
612854-63-4, DNA (Haemophilus influenzae gene murD)
                                                       612854-65-6,
DNA (Haemophilus influenzae gene murD)
                                         612854-67-8, DNA
(Escherichia coli gene murC) 612854-68-9, DNA (Escherichia coli
gene murC)
   (nucleotide sequence; cloning and phys. characterization of
   microbial polypeptides involved in membrane biogenesis
   and their use as antimicrobial targets)
3211-76-5, Selenomethionine
   (protein label for mass spectrometry; cloning
   and phys. characterization of microbial polypeptides
   involved in membrane biogenesis and their use as antimicrobial
   targets)
9014-08-8, Enolase
                     9027-73-0, 5'-Nucleotidase 9027-80-9, Adenine
phosphoribosyltransferase
   (protein-protein interactions of; cloning and phys.
   characterization of microbial polypeptides involved in
   membrane biogenesis and their use as antimicrobial targets)
612553-76-1
              612572-39-1
                            612572-40-4
                                          612572-41-5
                                                         612572-42-6
612572-43-7
              612572-44-8
                            612572-45-9
                                          612572-46-0
                                                         612572-47-1
612572-48-2
              612572-49-3
                            612572-50-6
                                          612572-51-7
                                                         612572-52-8
612572-53-9
              612572-54-0
                            612572-55-1
                                          612572-56-2
                                                        612572-57-3
612572-58-4
              612572-59-5
                            612572-60-8
                                          612572-61-9
                                                        612572-62-0
612572-63-1
              612572-64-2
                            612572-65-3
                                          612572-66-4
                                                        612572-67-5
612572-68-6
              612572-69-7
                            612572-70-0
                                          612572-71-1
                                                        612572-72-2
612572-74-4
              612572-75-5
                            612572-76-6
                                          612572-77-7
   (unclaimed nucleotide sequence; cloning and phys.
   characterization of microbial polypeptides involved in
   membrane biogenesis and their use as antimicrobial targets)
612572-73-3
   (unclaimed protein sequence; cloning and phys. characterization
   of microbial polypeptides involved in membrane
   biogenesis and their use as antimicrobial targets)
612542-37-7
              612542-38-8
                                          612542-40-2
                            612542-39-9
                                                        612542-41-3
612542-42-4
              612542-43-5
                            612542-44-6
                                          612542-45-7
                                                        612542-46-8
612542-47-9
              612542-48-0
                            612542-49-1
                                          612542-50-4
                                                        612542-51-5
612542-52-6
              612542-53-7
                            612542-54-8
                                          612542-55-9
                                                        612542-56-0
612542-57-1
              612542-58-2
                            612542-60-6
                                          612542-61-7
                                                        612542-62-8
612542-63-9
              612542-64-0
                            612542-65-1
                                          612542-66-2
                                                        612542-67-3
612542-68-4
              612542-69-5
                            612542-70-8
                                          612542-71-9
                                                        612542-72-0
612542-73-1
              612542-74-2
                            612542-75-3
                                          612542-76-4
                                                        612542-77-5
612542-78-6
              612542-79-7
                            612542-80-0
                                          612542-81-1
                                                        612542-82-2
```

IT

ΙΤ

ΙT

IT

ΙT

```
612542-83-3 612542-84-4 612542-85-5 612542-87-7 612542-89-9 612542-91-3 612542-93-5 612542-94-6 612542-95-7 612542-96-8 612542-97-9
```

(unclaimed sequence; cloning and phys. characterization of microbial **polypeptides** involved in membrane biogenesis and their use as antimicrobial targets)

L101 ANSWER 4 OF 28 HCA COPYRIGHT 2004 ACS on STN 139:319350 Cloning and physical characterization of microbial polypeptides involved in cellular transport and metabolism and their use as antimicrobial targets. Edwards, Aled; Dharamsi, Akil; Vedadi, Masoud; Li, Qin; Nethery, Kathleen; Mcdonald, Merry-lynn; Vallee, Francois; Awrey, Donald; Beattie, Bryan; Domagala, Megan; Mansoury, Kamran; Alam, Muhammad Zahoor; Ng, Ivy; Ouyang, Hui (Affinium Pharmaceuticals, Inc., Can.; et al.). PCT Int. Appl. WO 2003087146 A2 20031023, 204 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-CA482 20030408. PRIORITY: US 2002-PV370868 20020408; US 2002-PV371025 20020409; US 2002-PV371094 20020409; US 2002-PV370959 20020409; US 2002-PV371065 20020409. The present invention relates to polypeptide targets for AB pathogenic bacteria. Reliable, high throughput methods are developed to identify, express, and purify a no. of antimicrobial targets from Staphylococcus aureus, Escherichia coli, and Helicobacter pylori. The nucleic acid and amino acid sequences are provided for adenylate kinase, UDP-N-acetylglucosamine pyrophosphorylase, geranyltransferase (farnesyldiphosphate synthase), enoyl-(acyl carrier protein) reductase (NADH), and ribonucleoside diphosphate reductase .beta. subunit. The invention also provides bioinformatic, biochem. and biophys. characteristics of those polypeptides, in particular characterization by mass spectrometry, NMR spectrometry, and x-ray crystallog. ΙT 7782-39-0, Hydrogen-2, uses

(NMR isotope; cloning and phys. characterization of microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets)

RN 7782-39-0 HCA

CN Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME)

```
D-D
```

IT 666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3, Methanol-d4 865-49-6, Chloroform-d 917-96-4, Methyl-d3 isocyanide 1076-43-3, Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9 , Tetrahydrofuran-d8 1735-17-7, Cyclohexane-d12 2037-26-5 2206-27-1, Dimethyl sulfoxide-d6 2679-89-2, Diethyl-d10 ether 4472-41-7, N, N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Deuterium oxide 17222-37-6, Dimethyl-d6 ether (deuterium lock solvent for NMR spectroscopy; cloning and phys. characterization of microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets) RN 666-52-4 HCA CN 2-Propanone-1,1,1,3,3,3-d6 (9CI) (CA INDEX NAME) D3C-C-CD3 RN 811-98-3 HCA CN Methanol-d4 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 865-49-6 HCA CN Methane-d, trichloro- (9CI) (CA INDEX NAME)

RN 917-96-4 HCA CN Methane-d3, isocyano- (9CI) (CA INDEX NAME)

RN 1076-43-3 HCA CN Benzene-d6 (8CI, 9CI

Benzene-d6 (8CI, 9CI) (CA INDEX NAME)

$$\begin{array}{c} D \\ D \\ D \\ \end{array}$$

RN 1516-08-1 HCA

CN Ethanol-d6 (9CI) (CA INDEX NAME)

D3C-CD2-O-D

RN 1665-00-5 HCA

CN Methane-d2, dichloro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 1693-74-9 HCA

CN Furan-d4, tetrahydro-d4- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$$D \longrightarrow D$$

RN 1735-17-7 HCA

CN Cyclohexane-d12 (6CI, 8CI, 9CI) (CA INDEX NAME)

RN 2037-26-5 HCA

CN Benzene-d5, methyl-d3- (9CI) (CA INDEX NAME)

RN 2206-27-1 HCA

CN Methane-d3, sulfinylbis- (9CI) (CA INDEX NAME)

RN 2679-89-2 HCA

CN Ethane-d5, 2,2'-oxybis- (9CI) (CA INDEX NAME)

RN 4472-41-7 HCA

CN Formamide-1-d, N, N-di(methyl-d3) - (7CI, 8CI, 9CI) (CA INDEX NAME)

RN 7291-22-7 HCA

CN Pyridine-d5 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 7789-20-0 HCA Water-d2 (9CI) (CA INDEX NAME) CN

D- O- D

RN 17222-37-6 HCA

Methane-d3, oxybis- (9CI) (CA INDEX NAME) CN

D3C-0-CD3

IC ICM C07K014-31

C07K014-245; C07K014-205; C12N015-31; C12N015-62; C12Q001-68; ICS C12N015-11; C07K016-12; A61K038-16; A61K039-108; A61K039-085;

CC 7-2 (Enzymes)

Section cross-reference(s): 1, 3, 6, 10

essential protein pathogenic bacteria therapeutic target; sequence ST essential protein gene pathogenic bacteria; mass spectrometry essential protein pathogenic bacteria; NMR spectrometry essential protein pathogenic bacteria; xray crystallog essential protein pathogenic bacteria; cloning essential protein pathogenic bacteria

ΙΤ Antibacterial agents

Cryoprotectants

Crystallization

DNA sequences

Drug design

Drug screening

Drug targets

Epitopes

Escherichia coli

Helicobacter pylori

Mass spectrometry

Molecular cloning

NMR spectroscopy

Pathogenic bacteria

Protein sequences

Staphylococcus aureus

(cloning and phys. characterization of microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets)

Hydrocarbon oils ΙT

Polyoxyalkylenes, uses

(cryoprotectant; cloning and phys. characterization of microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets)

Solvents IT

6

(deuterium lock, for NMR spectroscopy; cloning and phys. characterization of microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets)

Fusion proteins (chimeric proteins) ΙT (for improved soly. or stability; cloning and phys. characterization of microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets)

Elements ΙT

(heavy, for mass spectrometry; cloning and phys. characterization of microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets)

Proteins ΙΤ

(in cellular transport and metab.; cloning and phys. characterization of microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets)

Molecular association ΙT

(protein-protein; cloning and phys. characterization of microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets)

Biological transport TT

Metabolism, microbial

(proteins involved in; cloning and phys. characterization of microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets)

Crystallography ΙΤ

(x-ray; cloning and phys. characterization of microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets)

7723-14-0, Phosphorus-31, uses 7440-23-5, Sodium-23, uses IT7727-37-9, Nitrogen-14, uses **7782-39-0**, Hydrogen-2, uses 7782-41-4, Fluorine-19, uses 10028-17-8, Hydrogen-3, uses 12184-88-2, Hydride 14390-96-6, Nitrogen-15, uses 14762-74-4, Carbon-13, uses (NMR isotope; cloning and phys. characterization of

¢

microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets) 612854-36-1P 612854-34-9P 612854-32-7P 612854-30-5P IT 612854-42**-**9P 612854-44-1P 612854-40**-**7P 612854-38**-**3P 612854-48-5P 612854-46-3P (amino acid sequence; cloning and phys. characterization of microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets) 9013-02-9P, Adenylate kinase 9023-06-7P, UDP-acetylglucosamine ΙΤ 37251-08-4P, Enoyl-(acyl carrier protein) pyrophosphorylase 50812-36-7P, Farnesyldiphosphate synthase (cloning and phys. characterization of microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets) 64-18-6, Formic acid, uses 56-81-5, Glycerol, uses ΙΤ Isopropanol, uses 77-92-9, Citric acid, uses 107-21-1, Ethylene 5683-44-3, 3-Methyl-2,4-pentanediol 25322-68-3, alvcol, uses Polyethylene glycol (cryoprotectant; cloning and phys. characterization of microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets) 666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3, ΙT Methanol-d4 865-49-6, Chloroform-d 917-96-4, Methyl-d3 isocyanide 1076-43-3, Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9 , Tetrahydrofuran-d8 1735-17-7, Cyclohexane-d12 2037-26-5 2206-27-1, Dimethyl sulfoxide-d6 2679-89-2, Diethyl-d10 ether 4472-41-7, N, N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Deuterium oxide 17222-37-6, Dimethyl-d6 ether (deuterium lock solvent for NMR spectroscopy; cloning and phys. characterization of microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets) 7429-91-6, Dysprosium, uses 7439-88-5, Iridium, uses 7439-90-9, ΙT 7439-91-0, Lanthanum, uses 7439-92-1, Lead, uses Krypton, uses 7439-94-3, Lutetium, uses 7439-97-6, Mercury, uses 7439-98-7, Molybdenum, uses 7440-00-8, Neodymium, uses 7440-04-2, Osmium, 7440-05-3, Palladium, uses 7440-06-4, Platinum, uses 7440-10-0, Praseodymium, uses 7440-15-5, Rhenium, uses 7440-19-9, 7440-16-6, Rhodium, uses 7440-18-8, Ruthenium, uses Samarium, uses 7440-22-4, Silver, uses 7440-24-6, Strontium, uses 7440-25-7, Tantalum, uses 7440-27-9, Terbium, uses 7440-28-0, Thallium, uses 7440-29-1, Thorium, uses 7440-30-4, Thulium, uses 7440-31-5, Tin, uses 7440-33-7, Tungsten, uses 7440-39-3, Barium, uses 7440-43-9, Cadmium, uses 7440-45-1, 7440-48-4, Cobalt, uses 7440-52-0, Erbium, uses Cerium, uses

```
Wallenhorst 10/045,170
7440-53-1, Europium, uses 7440-54-2, Gadolinium, uses
                                                         7440-57-5,
             7440-60-0, Holmium, uses 7440-61-1, Uranium, uses
Gold, uses
7440-63-3, Xenon, uses 7440-64-4, Ytterbium, uses
                                                     7553-56-2,
                                        7782-49-2, Selenium, uses
              7726-95-6, Bromine, uses
Iodine, uses
   (heavy atom for mass spectrometry; cloning
   and phys. characterization of microbial polypeptides
   involved in cellular transport and metab. and their use as
   antimicrobial targets)
59-67-6D, Nicotinic acid, derivs. 621-82-9D, Cinnamic acid,
derivs.
   (mass spectrometry of; cloning and phys.
   characterization of microbial polypeptides involved in
   cellular transport and metab. and their use as antimicrobial
   targets)
612854-29-2, DNA (Staphylococcus aureus gene adk) 612854-31-6, DNA
(Staphylococcus aureus gene adk) 612854-33-8, DNA (Helicobacter
                    612854-35-0, DNA (Helicobacter pylori gene glmU)
pylori gene glmU)
                                                612854-39-4, DNA
612854-37-2, DNA (Escherichia coli gene ispA)
(Escherichia coli gene ispA) 612854-41-8, DNA (Helicobacter pylori
            612854-43-0, DNA (Helicobacter pylori gene fabl)
                                                   612854-47-4, DNA
612854-45-2, DNA (Helicobacter pylori gene nrdB)
(Helicobacter pylori gene nrdB)
   (nucleotide sequence; cloning and phys. characterization of
   microbial polypeptides involved in cellular transport
```

ΙT

ΙT

IT

and metab. and their use as antimicrobial targets) 3211-76-5, Selenomethionine ΙT (protein label for mass spectrometry; cloning and phys. characterization of microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets)

612880-17-8 612880-20-3 612880-16-7 612880-15-6 612880-14-5 ΙT 612880-26-9 612880-25-8 612880-23-6 612880-22-5 612880-21-4 (unclaimed nucleotide sequence; cloning and phys. characterization of microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets)

612880-24-7 612880-19-0 612880-18-9 IT(unclaimed protein sequence; cloning and phys. characterization of microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets)

612805-53-5 612805-51-3 612805-52-4 612805-50-2 612805-49-9 612805-58-0 612805-57-9 612805-56-8 612805-55-7 612805-54-6 612805-60-4 612805-59-1

(unclaimed sequence; cloning and phys. characterization of microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets)

9047-64-7P, Ribonucleoside diphosphate reductase IT (.beta. subunit; cloning and phys. characterization of microbial polypeptides involved in cellular transport and metab. and their use as antimicrobial targets)

L101 ANSWER 5 OF 28 HCA COPYRIGHT 2004 ACS on STN 139:319349 Cloning and physical characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets. Edwards, Aled; Dharamsi, Akil; Vedadi, Masoud; Mcdonald, Merry-lynn; Li, Qin; Awrey, Donald; Beattie, Bryan (Affinium Pharmaceuticals, Inc., Can.). PCT Int. Appl. WO 2003087145 A2 20031023, 179 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-CA483 20030408. PRIORITY: US 2002-PV370806 20020408; US 2002-PV370978 20020409; US 2002-PV371009 20020409. The present invention relates to polypeptide targets for AΒ pathogenic bacteria. Reliable, high throughput methods are developed to identify, express, and purify a no. of antimicrobial targets from Escherichia coli and Pseudomonas aeruginosa. The nucleic acid and amino acid sequences are provided for RhlR and LasR homolog, autoinducer synthesis protein RhlI, and autoinducer synthesis protein LasI. The invention also provides bioinformatic, biochem. and biophys. characteristics of those polypeptides , in particular characterization by mass spectrometry, NMR spectrometry, and x-ray crystallog. 7782-39-0, Hydrogen-2, uses ΙT (NMR isotope; cloning and phys. characterization of

(NMR isotope; cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets)

RN 7782-39-0 HCA

CN Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME)

D-D

1T 666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3, Methanol-d4 865-49-6, Chloroform-d 917-96-4, Methyl-d3 isocyanide 1076-43-3, Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9, Tetrahydrofuran-d8 1735-17-7, Cyclohexane-d12 2037-26-5 2206-27-1, Dimethyl sulfoxide-d6

```
2679-89-2, Diethyl-d10 ether 4472-41-7,
    N, N-Dimethylformamide-d7 7291-22-7, Pyridine-d5
    7789-20-0, Deuterium oxide 17222-37-6,
    Dimethyl-d6 ether
        (deuterium lock solvent for NMR spectroscopy; cloning
       and phys. characterization of microbial polypeptides
       involved in quorum sensing and their use as antimicrobial
       targets)
    666-52-4 HCA
    2-Propanone-1,1,1,3,3,3-d6 (9CI) (CA INDEX NAME)
D3C-C-CD3
    811-98-3 HCA
    Methanol-d4 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)
D3C-0-D
     865-49-6 HCA
    Methane-d, trichloro- (9CI) (CA INDEX NAME)
   D
C1-C-C1
   Cl
     917-96-4 HCA
     Methane-d3, isocyano- (9CI) (CA INDEX NAME)
```

RN

CN

RN

CN

RN

CN

RN

CN

RN

CN

 $_{\mathrm{D3C}}-\mathrm{N}\overset{+}{=}\mathrm{C}^{-}$

1076-43-3 HCA

Benzene-d6 (8CI, 9CI) (CA INDEX NAME)

$$\begin{array}{c} D \\ D \\ D \end{array}$$

RN1516-08-1 HCA

Ethanol-d6 (9CI) (CA INDEX NAME) CN

D3C-CD2-O-D

1665-00-5 HCA RN

Methane-d2, dichloro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME) CN

1693-74-9 HCA RN

Furan-d4, tetrahydro-d4- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME) CN

$$D \longrightarrow D$$

1735-17-7 HCA RN

Cyclohexane-d12 (6CI, 8CI, 9CI) (CA INDEX NAME) CN

3

2037-26-5 HCA RN

Benzene-d5, methyl-d3- (9CI) (CA INDEX NAME) CN

2206-27-1 HCA RN

Methane-d3, sulfinylbis- (9CI) (CA INDEX NAME) CN

2679-89-2 HCA RN

Ethane-d5, 2,2'-oxybis- (9CI) (CA INDEX NAME) CN

4472-41-7 HCA RN

Formamide-1-d, N,N-di(methyl-d3)- (7CI, 8CI, 9CI) (CA INDEX NAME) CN

7291-22-7 HCA RN

Pyridine-d5 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME) CN

$$\begin{array}{c} D \\ \end{array}$$

7789-20-0 HCA RN

Water-d2 (9CI) (CA INDEX NAME) CN D— O— D 17222-37-6 HCA RN Methane-d3, oxybis- (9CI) (CA INDEX NAME) CN D3C-0-CD3 ICM C07K014-245 IC ICS C12N015-31; C12N015-62; G01N033-50; C07K014-21 7-2 (Enzymes) CC Section cross-reference(s): 1, 3, 6, 10 essential protein pathogenic bacteria therapeutic target; sequence ST essential protein gene pathogenic bacteria; mass spectrometry essential protein pathogenic bacteria; NMR spectrometry essential protein pathogenic bacteria; xray crystallog essential protein pathogenic bacteria; cloning essential protein pathogenic bacteria ΙΤ Proteins (RhlR and LasR homolog; cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets) Proteins ΙT (autoinducer synthesis LasI; cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets) Proteins ΙT (autoinducer synthesis RhlI; cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets) Antibacterial agents ΙT Cryoprotectants Crystallization DNA sequences Drug design Drug screening Drug targets Epitopes Escherichia coli Mass spectrometry Molecular cloning NMR spectroscopy Pathogenic bacteria Protein sequences Pseudomonas aeruginosa

(cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets)

Hydrocarbon oils ΙT

Polyoxyalkylenes, uses

(cryoprotectant; cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets)

ΙT Solvents

(deuterium lock, for NMR spectroscopy; cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets)

Fusion proteins (chimeric proteins) ΙT (for improved soly. or stability; cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets)

Elements TΤ

(heavy, for mass spectrometry; cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets)

ΙT Proteins

(in quorum sensing; cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets)

Molecular association ΙΤ

(protein-protein; cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets)

ΙT Ouorum sensing

(proteins involved in; cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets)

Crystallography ΙT

(x-ray; cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets)

7723-14-0, Phosphorus-31, uses 7440-23-5, Sodium-23, uses ΙΤ 7727-37-9, Nitrogen-14, uses **7782-39-0**, Hydrogen-2, uses 7782-41-4, Fluorine-19, uses 10028-17-8, Hydrogen-3, uses 12184-88-2, Hydride 14390-96-6, Nitrogen-15, uses Carbon-13, uses

(NMR isotope; cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets)

612554-26-4P, Protein (Escherichia coli gene sdiA) 612554-28-6P TΤ 612554-30-0P 612554-32-2P 612554-34-4P

(amino acid sequence; cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets)

IT 56-81-5, Glycerol, uses 64-18-6, Formic acid, uses 67-63-0, Isopropanol, uses 77-92-9, Citric acid, uses 107-21-1, Ethylene glycol, uses 5683-44-3, 3-Methyl-2,4-pentanediol 25322-68-3, Polyethylene glycol

(cryoprotectant; cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets)

666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3, Methanol-d4 865-49-6, Chloroform-d 917-96-4, Methyl-d3 isocyanide 1076-43-3, Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9, Tetrahydrofuran-d8 1735-17-7, Cyclohexane-d12 2037-26-5 2206-27-1, Dimethyl sulfoxide-d6 2679-89-2, Diethyl-d10 ether 4472-41-7, N,N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Deuterium oxide 17222-37-6, Dimethyl-d6 ether

ΙT

ΙT

ΙΤ

(deuterium lock solvent for NMR spectroscopy; cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets)

7429-91-6, Dysprosium, uses 7439-88-5, Iridium, uses 7439-90-9, Krypton, uses 7439-91-0, Lanthanum, uses 7439-92-1, Lead, uses 7439-94-3, Lutetium, uses 7439-97-6, Mercury, uses 7439-98-7, 7440-00-8, Neodymium, uses 7440-04-2, Osmium, Molybdenum, uses uses 7440-05-3, Palladium, uses 7440-06-4, Platinum, uses 7440-10-0, Praseodymium, uses 7440-15-5, Rhenium, uses 7440-16-6, Rhodium, uses 7440-18-8, Ruthenium, uses 7440-19-9, Samarium, uses 7440-22-4, Silver, uses 7440-24-6, Strontium, 7440-25-7, Tantalum, uses 7440-27-9, Terbium, uses uses 7440-28-0, Thallium, uses 7440-29-1, Thorium, uses 7440-31-5, Tin, uses 7440-33-7, Tungsten, uses Thulium, uses 7440-39-3, Barium, uses 7440-43-9, Cadmium, uses 7440-45-1, 7440-48-4, Cobalt, uses 7440-52-0, Erbium, uses Cerium, uses 7440-53-1, Europium, uses 7440-54-2, Gadolinium, uses 7440-57-5, 7440-60-0, Holmium, uses 7440-61-1, Uranium, uses Gold, uses 7440-63-3, Xenon, uses 7440-64-4, Ytterbium, uses 7553-56-2, Iodine, uses 7726-95-6, Bromine, uses 7782-49-2, Selenium, uses (heavy atom for mass spectrometry; cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial

59-67-6D, Nicotinic acid, derivs. 621-82-9D, Cinnamic acid, derivs.

(mass spectrometry of; cloning and phys.

characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets)

IT 612554-25-3, DNA (Escherichia coli gene sdiA) 612554-27-5, DNA (Pseudomonas aeruginosa gene rhlI) 612554-29-7, DNA (Pseudomonas aeruginosa gene rhlI) 612554-31-1, DNA (Pseudomonas aeruginosa gene lasI) 612554-33-3, DNA (Pseudomonas aeruginosa gene lasI) (nucleotide sequence; cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets)

IT 3211-76-5, Selenomethionine

IT 612574-07-9 612574-08-0 612574-10-4 612574-11-5 612574-12-6 612574-13-7

(unclaimed nucleotide sequence; cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets)

1T 612574-09-1 (unclaimed protein sequence; cloning and phys. characterization of microbial polypeptides involved in quorum sensing

ΙT

and their use as antimicrobial targets)
612507-63-8 612507-65-0 612507-69-4 612507-73-0 612507-78-5
612507-85-4 612507-90-1 612507-96-7

(unclaimed sequence; cloning and phys. characterization of microbial polypeptides involved in quorum sensing and their use as antimicrobial targets)

L101 ANSWER 6 OF 28 HCA COPYRIGHT 2004 ACS on STN 139:319345 Cloning and physical characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets. Edwards, Aled; Dharamsi, Akil; Vedadi, Masoud; Domagala, Megan; Kanagarajah, Dhushy; Awrey, Donald; Beattie, Bryan; Mcdonald, Merry-Lynn; Nethery, Kathleen; Mansoury, Kamran; Ouyang, Hui (Affinium Pharmaceuticals, Inc., Can.). Int. Appl. WO 2003085103 A2 20031016, 212 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-CA472 20030404. PRIORITY: US 2002-PV369822 20020404; US 2002-PV370849 20020408; US 2002-PV370854 20020408; US 2002-PV370860 20020408; US 2002-PV371066 20020409; US

2002-PV371151 20020409. The present invention relates to polypeptide targets for AΒ pathogenic bacteria. Reliable, high throughput methods are developed to identify, express, and purify a no. of antimicrobial targets from Staphylococcus aureus, Escherichia coli, Streptococcus pneumoniae, and Pseudomonas aeruginosa. The nucleic acid and amino acid sequences are provided for cell division protein FtsA, GTP-binding protein Era, cell division protein FtsZ, and the gene yihA conserved hypothetical protein from Escherichia coli and Pseudomonas aeruginosa. The invention also provides bioinformatic, biochem. and biophys. characteristics of those polypeptides , in particular characterization by mass spectrometry, NMR spectrometry, and x-ray crystallog. ΙΤ 7782-39-0, Hydrogen-2, uses (NMR isotope; cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets) 7782-39-0 HCA RN Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME) CND-- D 666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3, ΙT Methanol-d4 865-49-6, Chloroform-d 917-96-4, Methyl-d3 isocyanide 1076-43-3, Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9 , Tetrahydrofuran-d8 1735-17-7, Cyclohexane-d12 2037-26-5 2206-27-1, Dimethyl sulfoxide-d6 2679-89-2, Diethyl-d10 ether 4472-41-7, N, N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Deuterium oxide 17222-37-6, Dimethyl-d6 ether (deuterium lock solvent for NMR spectroscopy; cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets) 666-52-4 HCA RN 2-Propanone-1,1,1,3,3,3-d6 (9CI) (CA INDEX NAME) CN D3C-C-CD3

Methanol-d4 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN

CN

811-98-3 HCA

D3C-O-D

RN 865-49-6 HCA

CN Methane-d, trichloro- (9CI) (CA INDEX NAME)

RN 917-96-4 HCA

CN Methane-d3, isocyano- (9CI) (CA INDEX NAME)

$$D3C-N \stackrel{+}{=} C^-$$

RN 1076-43-3 HCA

CN Benzene-d6 (8CI, 9CI) (CA INDEX NAME)

RN 1516-08-1 HCA

CN Ethanol-d6 (9CI) (CA INDEX NAME)

D3C-CD2-O-D

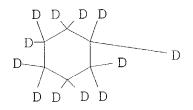
RN 1665-00-5 HCA

CN Methane-d2, dichloro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 1693-74-9 HCA CN Furan-d4, tetrahydro-d4- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$$D \longrightarrow D \longrightarrow D$$

RN 1735-17-7 HCA CN Cyclohexane-d12 (6CI, 8CI, 9CI) (CA INDEX NAME)



RN 2037-26-5 HCA CN Benzene-d5, methyl-d3- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} D & CD3 \\ \hline D & D \\ \end{array}$$

RN 2206-27-1 HCA CN Methane-d3, sulfinylbis- (9CI) (CA INDEX NAME)

2679-89-2 HCA RN

Ethane-d5, 2,2'-oxybis- (9CI) (CA INDEX NAME) CN

D3C-CD2-O-CD2-CD3

4472-41-7 HCA RN

Formamide-1-d, N,N-di(methyl-d3)- (7CI, 8CI, 9CI) (CA INDEX NAME) CN

7291-22-7 HCA RN

Pyridine-d5 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME) CN

7789-20-0 HCA RN

Water-d2 (9CI) (CA INDEX NAME) CN

D-- O-- D

17222-37-6 HCA RN

Methane-d3, oxybis- (9CI) (CA INDEX NAME) CN

D3C-0-CD3

ICM C12N009-10 IC

ICS G06F017-50

CC7-2 (Enzymes)

Section cross-reference(s): 1, 3, 6, 10

essential protein pathogenic bacteria therapeutic target; sequence ST

Wallenhorst 10/045,170 essential protein gene pathogenic bacteria; mass spectrometry essential protein pathogenic bacteria; NMR spectrometry essential protein pathogenic bacteria; xray crystallog essential protein pathogenic bacteria; cloning essential protein pathogenic bacteria Molecular chaperones (DnaK, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets) Proteins (GTP-binding, gene Era; cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets) Heat-shock proteins (HSP 70, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets) Ribosomal proteins (L13, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets) Ribosomal proteins (L14, protein-protein interactions of; cloning and phys.

ΤТ

ΙΤ

ΙΤ

ΙΤ

ΙT characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets)

Ribosomal proteins ΙT (L2, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets)

Ribosomal proteins IT(L5, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets)

Ribosomal proteins ΙT (S11, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets) ΙT

Ribosomal proteins (S19, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets)

Ribosomal proteins ΙT (S7, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets)

Ribosomal proteins ΙT (S9, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in

nucleotide hydrolysis and their use as antimicrobial targets) ΙT Antibacterial agents Cryoprotectants Crystallization DNA sequences Drug design Drug screening Drug targets Epitopes Escherichia coli Mass spectrometry Molecular cloning NMR spectroscopy Pathogenic bacteria Protein sequences Pseudomonas aeruginosa Staphylococcus aureus Streptococcus pneumoniae (cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets) Hydrocarbon oils ΙT Polyoxyalkylenes, uses (cryoprotectant; cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets) ΙT Solvents (deuterium lock, for NMR spectroscopy; cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets) Fusion proteins (chimeric proteins) ΙT (for improved soly. or stability; cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets) TΤ Proteins (ftsA; cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets) ΙΤ Proteins (ftsZ; cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets) ΙT (gene yihA; cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets) ITElements

ΙT

ΙΤ

ΙT

ΙT

IT

ΙT

ΤТ

ΤТ

```
(heavy, for mass spectrometry; cloning and
   phys. characterization of microbial polypeptides
   involved in nucleotide hydrolysis and their use as antimicrobial
   targets)
Proteins
   (in nucleotide hydrolysis; cloning and phys. characterization of
   microbial polypeptides involved in nucleotide
   hydrolysis and their use as antimicrobial targets)
Molecular association
   (protein-protein; cloning and phys. characterization of microbial
   polypeptides involved in nucleotide hydrolysis and their
   use as antimicrobial targets)
Nucleotides, biological studies
   (proteins involved in hydrolysis of; cloning and phys.
   characterization of microbial polypeptides involved in
   nucleotide hydrolysis and their use as antimicrobial targets)
Crystallography
   (x-ray; cloning and phys. characterization of microbial
   polypeptides involved in nucleotide hydrolysis and their
   use as antimicrobial targets)
7440-23-5, Sodium-23, uses
                           7723-14-0, Phosphorus-31, uses
7727-37-9, Nitrogen-14, uses 7782-39-0, Hydrogen-2, uses
7782-41-4, Fluorine-19, uses 10028-17-8, Hydrogen-3, uses
12184-88-2, Hydride 14390-96-6, Nitrogen-15, uses
                                                    14762-74-4,
Carbon-13, uses
   (NMR isotope; cloning and phys. characterization of
   microbial polypeptides involved in nucleotide
   hydrolysis and their use as antimicrobial targets)
612853-29-9P
               612853-31-3P
                              612853-33-5P
                                             612853-35-7P
               612853-39-1P
                              612853-41-5P, Protein (Escherichia
612853-37-9P
                  612853-43-7P, Protein (Escherichia coli gene yihA)
coli gene yihA)
              612853-48-2P 612853-50-6P
612853-45-9P
   (amino acid sequence; cloning and phys. characterization of
   microbial polypeptides involved in nucleotide
   hydrolysis and their use as antimicrobial targets)
56-81-5, Glycerol, uses 64-18-6, Formic acid, uses
                                                       67-63-0,
                                                107-21-1, Ethylene
                   77-92-9, Citric acid, uses
Isopropanol, uses
               5683-44-3, 3-Methyl-2,4-pentanediol
                                                     25322-68-3,
glycol, uses
Polyethylene glycol
   (cryoprotectant; cloning and phys. characterization of microbial
   polypeptides involved in nucleotide hydrolysis and their
   use as antimicrobial targets)
666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3,
Methanol-d4 865-49-6, Chloroform-d 917-96-4,
Methyl-d3 isocyanide 1076-43-3, Benzene-d6
1516-08-1, Ethanol-d6 1665-00-5 1693-74-9
, Tetrahydrofuran-d8 1735-17-7, Cyclohexane-d12
```

2037-26-5 2206-27-1, Dimethyl sulfoxide-d6

2679-89-2, Diethyl-d10 ether 4472-41-7, N, N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Deuterium oxide 17222-37-6, Dimethyl-d6 ether

(deuterium lock solvent for NMR spectroscopy; cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets)

7439-88-5, Iridium, uses 7429-91-6, Dysprosium, uses ΙΤ Krypton, uses 7439-91-0, Lanthanum, uses 7439-92-1, Lead, uses 7439-94-3, Lutetium, uses 7439-97-6, Mercury, uses 7439-98-7, Molybdenum, uses 7440-00-8, Neodymium, uses 7440-04-2, Osmium, 7440-05-3, Palladium, uses 7440-06-4, Platinum, uses 7440-10-0, Praseodymium, uses 7440-15-5, Rhenium, uses 7440-16-6, Rhodium, uses 7440-18-8, Ruthenium, uses 7440-19-9, Samarium, uses 7440-22-4, Silver, uses 7440-24-6, Strontium, 7440-25-7, Tantalum, uses 7440-27-9, Terbium, uses 7440-28-0, Thallium, uses 7440-29-1, Thorium, uses 7440-30-4, 7440-31-5, Tin, uses 7440-33-7, Tungsten, uses Thulium, uses 7440-45-1, 7440-39-3, Barium, uses 7440-43-9, Cadmium, uses Cerium, uses 7440-48-4, Cobalt, uses 7440-52-0, Erbium, uses 7440-53-1, Europium, uses 7440-54-2, Gadolinium, uses 7440-57-5, 7440-60-0, Holmium, uses 7440-61-1, Uranium, uses Gold, uses 7440-64-4, Ytterbium, uses 7440-63-3, Xenon, uses 7553-56-2, 7782-49-2, Selenium, uses Iodine, uses 7726-95-6, Bromine, uses (heavy atom for mass spectrometry; cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial

59-67-6D, Nicotinic acid, derivs. 621-82-9D, Cinnamic acid, ΙT derivs.

(mass spectrometry of; cloning and phys. characterization of microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets) 612853-28-8, DNA (Streptococcus pneumoniae gene ftsA) 612853-30-2, ΙT 612853-32-4, DNA DNA (Streptococcus pneumoniae gene ftsA) (Staphylococcus aureus gene era) 612853-34-6, DNA (Staphylococcus aureus gene era) 612853-36-8, DNA (Streptococcus pneumoniae gene 612853-38-0, DNA (Streptococcus pneumoniae gene ftsZ) 612853-40-4, DNA (Escherichia coli gene yihA) 612853-42-6, DNA 612853-44-8, DNA (Pseudomonas (Escherichia coli gene yihA) 612853-46-0, DNA (Pseudomonas aeruginosa aeruginosa gene yihA) gene yihA) 612853-47-1, DNA (Streptococcus pneumoniae gene era) 612853-49-3, DNA (Streptococcus pneumoniae gene era) (nucleotide sequence; cloning and phys. characterization of

microbial polypeptides involved in nucleotide hydrolysis and their use as antimicrobial targets)

3211-76-5, Selenomethionine

ΙT

```
(protein label for mass spectrometry; cloning
        and phys. characterization of microbial polypeptides
        involved in nucleotide hydrolysis and their use as antimicrobial
                         9055-66-7, Phenylalanyl-tRNA synthetase
ΙT
     9014-08-8, Enolase
     9068-08-0, Formate acetyltransferase
        (protein-protein interactions of; cloning and phys.
        characterization of microbial polypeptides involved in
        nucleotide hydrolysis and their use as antimicrobial targets)
                                 612865-92-6
                                               612865-93-7
                   612865-90-4
ΙΤ
     612865-89-1
                   612865-97-1
                                 612865-98-2
                                               612865-99-3
                                                             612866-00-9
     612865-96-0
     612866-01-0
                   612866-02-1
        (unclaimed nucleotide sequence; cloning and phys.
        characterization of microbial polypeptides involved in
        nucleotide hydrolysis and their use as antimicrobial targets)
                   612865-94-8
     612865-91-5
ΙT
        (unclaimed protein sequence; cloning and phys. characterization
        of microbial polypeptides involved in nucleotide
        hydrolysis and their use as antimicrobial targets)
ΙT
     612817-60-4
                   612817-61-5
                                 612817-62-6
                                               612817-63-7
                                                             612817-64-8
                                 612817-67-1
                                               612817-68-2
                                                             612817-69-3
     612817-65-9
                   612817-66-0
                   612817-71-7
                                                             612817-74-0
     612817-70-6
                                 612817-72-8
                                               612817-73-9
     612817-75-1
        (unclaimed sequence; cloning and phys. characterization of
        microbial polypeptides involved in nucleotide
```

hydrolysis and their use as antimicrobial targets)

L101 ANSWER 7 OF 28 HCA COPYRIGHT 2004 ACS on STN 139:319344 Cloning and physical characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets. Edwards, Aled; Dharamsi, Akil; Vedadi, Masoud; Domagala, Megan; Nethery, Kathleen; Awrey, Donald; Beattie, Bryan; Mcdonald, Merry-Lynn; Houston, Simon; Arrowsmith, Cheryl; Mansoury, Kamran; Ouyang, Hui; Kanagarajah, Dhushy; Ng, Ivy; Vallee, Francois (Affinium Pharmaceuticals, Inc., Can.). PCT Int. Appl. WO 2003084987 A2 20031016, 289 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, (English). CODEN: PIXXD2. APPLICATION: WO 2003-CA465 TD, TG, TR. 20030404. PRIORITY: US 2002-PV370060 20020404; US 2002-PV369831 20020404; US 2002-PV369819 20020404; US 2002-PV369826 20020404; US 2002-PV370852 20020408; US 2002-PV370681 20020408; US 2002-PV371014

20020409; US 2002-PV371180 20020409; US 2002-PV371008 20020409; US 2002-PV371114 20020409; US 2002-PV371189 20020409; US 2002-PV371064 20020409.

AB The present invention relates to polypeptide targets for pathogenic bacteria. Reliable, high throughput methods are developed to identify, express, and purify a no. of antimicrobial targets from Staphylococcus aureus, Escherichia coli, Streptococcus pneumoniae, Helicobacter pylori, and Pseudomonas aeruginosa. The nucleic acid and amino acid sequences are provided for GroES protein, transcription termination factor NusG, GrpE protein, RNA polymerase .alpha. subunit, prolyl-tRNA synthetase, seryl-tRNA synthetase, and L-Cysteine desulfurase. The invention also provides bioinformatic, biochem. and biophys. characteristics of those polypeptides, in particular characterization by mass spectrometry, NMR spectrometry, and x-ray crystallog.

IT 7782-39-0, Hydrogen-2, uses

(NMR isotope; cloning and phys. characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

RN 7782-39-0 HCA

CN Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME)

D— D

IT 666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3,
 Methanol-d4 865-49-6, Chloroform-d 917-96-4,
 Methyl-d3 isocyanide 1076-43-3, Benzene-d6
 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9
 , Tetrahydrofuran-d8 1735-17-7, Cyclohexane-d12
 2037-26-5 2206-27-1, Dimethyl sulfoxide-d6
 2679-89-2, Diethyl-d10 ether 4472-41-7,
 N,N-Dimethylformamide-d7,7291-22-7, Pyridine-d5
 7789-20-0, Deuterium oxide 17222-37-6,
 Dimethyl-d6 ether
 (deuterium lock solvent for NMR spectroscopy; cloning)

(deuterium lock solvent for NMR spectroscopy; cloning and phys. characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

RN 666-52-4 HCA

CN 2-Propanone-1,1,1,3,3,3-d6 (9CI) (CA INDEX NAME)

D3C-C-CD3

RN 811-98-3 HCA

CN Methanol-d4 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

D3C-O-D

RN 865-49-6 HCA

CN Methane-d, trichloro- (9CI) (CA INDEX NAME)

RN 917-96-4 HCA

CN Methane-d3, isocyano- (9CI) (CA INDEX NAME)

RN 1076-43-3 HCA

CN Benzene-d6 (8CI, 9CI) (CA INDEX NAME)

$$\begin{array}{c} D \\ D \\ D \\ \end{array}$$

RN 1516-08-1 HCA

CN Ethanol-d6 (9CI) (CA INDEX NAME)

D3C-CD2-O-D

RN 1665-00-5 HCA

CN Methane-d2, dichloro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 1693-74-9 HCA

CN Furan-d4, tetrahydro-d4- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 1735-17-7 HCA

CN Cyclohexane-d12 (6CI, 8CI, 9CI) (CA INDEX NAME)

RN 2037-26-5 HCA

CN Benzene-d5, methyl-d3- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} D & & \\ \hline D & & \\ D & & \\ \end{array}$$

RN 2206-27-1 HCA

CN Methane-d3, sulfinylbis- (9CI) (CA INDEX NAME)

RN 2679-89-2 HCA

CN Ethane-d5, 2,2'-oxybis- (9CI) (CA INDEX NAME)

D3C-CD2-O-CD2-CD3

RN 4472-41-7 HCA

CN Formamide-1-d, N, N-di(methyl-d3) - (7CI, 8CI, 9CI) (CA INDEX NAME)

RN 7291-22-7 HCA

CN Pyridine-d5 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$$\begin{array}{c} D \\ \end{array}$$

RN 7789-20-0 HCA

CN Water-d2 (9CI) (CA INDEX NAME)

D- O- D

RN 17222-37-6 HCA

CN Methane-d3, oxybis- (9CI) (CA INDEX NAME)

D3C-0-CD3

IC ICM C07K014-00

CC 7-2 (Enzymes)

Section cross-reference(s): 1, 3, 6, 10

ST essential protein pathogenic bacteria therapeutic target; sequence essential protein gene pathogenic bacteria; mass

spectrometry essential protein pathogenic

bacteria; NMR spectrometry essential protein

pathogenic bacteria; xray crystallog essential protein pathogenic

bacteria; cloning essential protein pathogenic bacteria

IT Molecular chaperones

(DnaK, protein-protein interactions of; cloning and phys. characterization of microbial **polypeptides** involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

IT Molecular chaperones

(GroES; cloning and phys. characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

IT Proteins

(GrpE; cloning and phys. characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

IT Heat-shock proteins

(HSP 70, protein-protein interactions of; cloning and phys. characterization of microbial **polypeptides** involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

IT Ribosomal proteins

(L1, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

IT Antibacterial agents

Cryoprotectants

Crystallization

DNA sequences

Drug design

Drug screening

Drug targets

Epitopes

Escherichia coli

Helicobacter pylori

Mass spectrometry

Molecular cloning

NMR spectroscopy

Pathogenic bacteria

Protein sequences

Pseudomonas aeruginosa

Staphylococcus aureus

Streptococcus pneumoniae

(cloning and phys. characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

IT Hydrocarbon oils

Polyoxyalkylenes, uses

(cryoprotectant; cloning and phys. characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

IT Solvents

(deuterium lock, for NMR spectroscopy; cloning and phys. characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

IT Fusion proteins (chimeric proteins)
(for improved soly. or stability; cloning and phys.

characterization of microbial **polypeptides** involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

IT Transcription factors

(gene nusG; cloning and phys. characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

IT Elements

(heavy, for mass spectrometry; cloning and phys. characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

IT Proteins

(in nucleic acid synthesis and processing; cloning and phys. characterization of microbial **polypeptides** involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

IT Molecular association

(protein-protein; cloning and phys. characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

IT Crystallography

(x-ray; cloning and phys. characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

IT Transcription factors

(.rho., protein-protein interactions of; cloning and phys. characterization of microbial **polypeptides** involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

TT 7440-23-5, Sodium-23, uses 7723-14-0, Phosphorus-31, uses 7727-37-9, Nitrogen-14, uses **7782-39-0**, Hydrogen-2, uses 7782-41-4, Fluorine-19, uses 10028-17-8, Hydrogen-3, uses 12184-88-2, Hydride 14390-96-6, Nitrogen-15, uses 14762-74-4, Carbon-13, uses

(NMR isotope; cloning and phys. characterization of

```
microbial polypeptides involved in nucleic acid
        synthesis and processing and their use as antimicrobial targets)
ΙT
     612813-91-9
                   612866-19-0
                                 612866-20-3
        (Unclaimed; cloning and phys. characterization of microbial
        polypeptides involved in nucleic acid synthesis and
        processing and their use as antimicrobial targets)
ΙT
     612853-52-8P
                    612853-54-0P
                                   612853-56-2P
                                                  612853-58-4P
     612853-60-8P 612853-62-0P
                                   612853-64-2P 612853-66-4P
     612853-68-6P 612853-70-0P 612853-72-2P 612853-74-4P
     612853-76-6P 612853-79-9P
                                   612853-81-3P
                                                  612853-83-5P
     612853-85-7P
                    612853-87-9P
                                   612853-89-1P
        (amino acid sequence; cloning and phys. characterization of
        microbial polypeptides involved in nucleic acid
        synthesis and processing and their use as antimicrobial targets)
ΙT
     9023-48-7P, Seryl-tRNA synthetase
                                         9055-68-9P, Prolyl-tRNA
                  149371-08-4P, Cysteine desulfurase
        (cloning and phys. characterization of microbial
        polypeptides involved in nucleic acid synthesis and
        processing and their use as antimicrobial targets)
     56-81-5, Glycerol, uses 64-18-6, Formic acid, uses
IT
     Isopropanol, uses
                        77-92-9, Citric acid, uses 107-21-1, Ethylene
     glycol, uses
                    5683-44-3, 3-Methyl-2, 4-pentanediol
                                                         25322-68-3,
     Polyethylene glycol
        (cryoprotectant; cloning and phys. characterization of microbial
        polypeptides involved in nucleic acid synthesis and
        processing and their use as antimicrobial targets)
ΙT
     666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3,
     Methanol-d4 865-49-6, Chloroform-d 917-96-4,
    Methyl-d3 isocyanide 1076-43-3, Benzene-d6
     1516-08-1, Ethanol-d6 1665-00-5 1693-74-9
     , Tetrahydrofuran-d8 1735-17-7, Cyclohexane-d12
     2037-26-5 2206-27-1, Dimethyl sulfoxide-d6
     2679-89-2, Diethyl-d10 ether 4472-41-7,
    N, N-Dimethylformamide-d7 7291-22-7, Pyridine-d5
     7789-20-0, Deuterium oxide 17222-37-6,
    Dimethyl-d6 ether
        (deuterium lock solvent for NMR spectroscopy; cloning
        and phys. characterization of microbial polypeptides
        involved in nucleic acid synthesis and processing and their use
        as antimicrobial targets)
     9073-60-3, Metallo-.beta.-lactamase
ΙΤ
        (family member, protein-protein interactions of; cloning and
       phys. characterization of microbial polypeptides
        involved in nucleic acid synthesis and processing and their use
       as antimicrobial targets)
IT
    7429-91-6, Dysprosium, uses
                                  7439-88-5, Iridium, uses 7439-90-9,
    Krypton, uses 7439-91-0, Lanthanum, uses 7439-92-1, Lead, uses
    7439-94-3, Lutetium, uses 7439-97-6, Mercury, uses
                                                          7439-98-7,
```

7440-00-8, Neodymium, uses 7440-04-2, Osmium, Molybdenum, uses uses 7440-05-3, Palladium, uses 7440-06-4, Platinum, uses 7440-10-0, Praseodymium, uses 7440-15-5, Rhenium, uses 7440-16-6, Rhodium, uses 7440-18-8, Ruthenium, uses 7440-19-9, Samarium, uses 7440-22-4, Silver, uses 7440-24-6, Strontium, 7440-25-7, Tantalum, uses 7440-27-9, Terbium, uses 7440-28-0, Thallium, uses 7440-29-1, Thorium, uses 7440-30-4, Thulium, uses 7440-31-5, Tin, uses 7440-33-7, Tungsten, uses 7440-39-3, Barium, uses 7440-43-9, Cadmium, uses 7440-45-1, 7440-48-4, Cobalt, uses 7440-52-0, Erbium, uses Cerium, uses 7440-53-1, Europium, uses 7440-54-2, Gadolinium, uses Gold, uses 7440-60-0, Holmium, uses 7440-61-1, Uranium, uses 7440-63-3, Xenon, uses 7440-64-4, Ytterbium, uses 7553-56-2, Iodine, uses 7726-95-6, Bromine, uses 7782-49-2, Selenium, uses (heavy atom for mass spectrometry; cloning and phys. characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

IT 59-67-6D, Nicotinic acid, derivs. 621-82-9D, Cinnamic acid, derivs.

(mass spectrometry of; cloning and phys. characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

ΙT 612853-51-7, DNA (Staphylococcus aureus gene groES) 612853-53-9, DNA (Pseudomonas aeruginosa gene groES) 612853-55-1, DNA (Helicobacter pylori gene groES) 612853-57-3, DNA (Escherichia coli gene nusG) 612853-59-5, DNA (Staphylococcus aureus gene grpE) 612853-61-9, DNA (Staphylococcus aureus gene grpE) 612853-63-1, DNA (Helicobacter pylori gene nusG) 612853-65-3, DNA (Helicobacter 612853-67-5 pylori gene nusG) 612853-69-7 612853-71-1, DNA (Helicobacter pylori gene rpoA) 612853-73-3, DNA (Helicobacter pylori gene rpoA) 612853-75-5, DNA (Staphylococcus aureus gene 612853-77-7, DNA (Staphylococcus aureus gene rpoA) 612853-78-8, DNA (Helicobacter pylori gene pros) 612853-80-2, DNA 612853-82-4, DNA (Streptococcus (Helicobacter pylori gene proS) pneumoniae gene serS) 612853-84-6, DNA (Streptococcus pneumoniae gene serS) 612853-86-8, DNA (Pseudomonas aeruginosa gene iscS) 612853-88-0, DNA (Pseudomonas aeruginosa gene iscS)

(nucleotide sequence; cloning and phys. characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets) 3211-76-5, Selenomethionine

(protein label for mass spectrometry; cloning and phys. characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

IT 9012-90-2, DNA polymerase

ΙT

(protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets) IT612866-21-4 612866-22-5 612866-24-7 612866-25-8 612866-26-9 612866-27-0 612866-28-1 612866-29-2 612866-30-5 612866-31-6 (unclaimed nucleotide sequence; cloning and phys. characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets) ΙT 612813-60-2 612813-58-8 612813-62-4 612813-63-5 612813-64-6 612813-67-9 612813-69-1 612813-71-5 612813-73-7 612813-75-9 612813-79-3 612813-77-1 612813-81-7 612813-83-9 612813-85-1 612813-87-3 612813-89-5 612813-93-1 612813-95-3 612813-97-5 612813-99-7 612814-01-4 612814-03-6 612814-05-8 612814-07-0 612814-13-8 612814-09-2 612814-11-6 612814-15-0 612814-17-2 612814-19-4 612814-21-8 612814-23-0 612866-03-2 612866-04-3 612866-05-4 612866-08-7 612866-06-5 612866-07-6 612866-09-8 612866-10-1 612866-12-3 612866-13-4 612866-14-5 612866-15-6 612866-16-7 612866-17-8 612866-18-9 612866-23-6 (unclaimed sequence; cloning and phys. characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets) ΙΤ 9014-24-8P, RNA polymerase (.alpha. subunit; cloning and phys. characterization of microbial polypeptides involved in nucleic acid synthesis and processing and their use as antimicrobial targets)

L101 ANSWER 8 OF 28 HCA COPYRIGHT 2004 ACS on STN 139:319343 Cloning and physical characterization of microbial polypeptides involved in cellular metabolism and their use as antimicrobial targets. Edwards, Aled; Dharamsi, Akil; Vedadi, Masoud; Domagala, Megan; Kanagarajah, Dhushy; Ouyang, Hui; Houston, Simon; Awrey, Donald; Beattie, Bryan; Nethery, Kathleen; Mansoury, Kamran; Buzadzija, Kristina; Ng, Ivy; Mcdonald, Merry-lynn; Richards, Dawn; Thalakada, Rosanne; Virag, Cristina; Alam, Muhammad Zahoor; Canadien, Veronica (Affinium Pharmaceuticals, Inc., Can.). PCT Int. Appl. WO 2003084986 A2 20031016, 285 pp. DESIGNATED AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, STATES: W: CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-CA464 20030404. PRIORITY: US 2002-PV369817 20020404; US 2002-PV370102 20020404; US

2002-PV370820 20020408; US 2002-PV370859 20020408; US 2002-PV370778 20020408; US 2002-PV370792 20020408; US 2002-PV371140 20020409; US 2002-PV386018 20020605; US 2002-PV386430 20020606; US 2002-PV436842 20021227; US 2002-PV436987 20021230.

The present invention relates to polypeptide targets for pathogenic bacteria. Reliable, high throughput methods are developed to identify, express, and purify a no. of antimicrobial targets from Staphylococcus aureus, Escherichia coli, Streptococcus pneumoniae, Haemophilus influenzae, and Pseudomonas aeruginosa. The nucleic acid and amino acid sequences are provided for ribulose phosphate 3-epimerase, acetyl-CoA carboxylase/transferase .beta. subunit, DNA gyrase subunit B, biotin carboxylase, riboflavin kinase/FAD synthase, phosphopantetheine adenylyltransferase, inorg. pyrophosphatase, and phosphoglucosamine mutase. The invention also provides bioinformatic, biochem. and biophys. characteristics of those polypeptides, in particular characterization by mass spectrometry, NMR spectrometry, and x-ray crystallog.

IT 7782-39-0, Hydrogen-2, uses

(NMR isotope; cloning and phys. characterization of microbial polypeptides involved in cellular metab. and their use as antimicrobial targets)

RN 7782-39-0 HCA

CN Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME)

D— D

IT 666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3, Methanol-d4 865-49-6, Chloroform-d 917-96-4, Methyl-d3 isocyanide 1076-43-3, Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9, Tetrahydrofuran-d8 1735-17-7, Cyclohexane-d12 2037-26-5 2206-27-1, Dimethyl sulfoxide-d6 2679-89-2, Diethyl-d10 ether 4472-41-7, N,N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Deuterium oxide 17222-37-6, Dimethyl-d6 ether (deuterium lock solvent for NMR spectroscopy

(deuterium lock solvent for NMR spectroscopy; cloning and phys. characterization of microbial polypeptides involved in cellular metab. and their use as antimicrobial targets)

RN 666-52-4 HCA

CN 2-Propanone-1,1,1,3,3,3-d6 (9CI) (CA INDEX NAME)

RN 811-98-3 HCA

CN Methanol-d4 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

D3C-O-D

RN 865-49-6 HCA

CN Methane-d, trichloro- (9CI) (CA INDEX NAME)

RN 917-96-4 HCA

CN Methane-d3, isocyano- (9CI) (CA INDEX NAME)

$$D_3C - N \stackrel{+}{=} C^-$$

RN 1076-43-3 HCA

CN Benzene-d6 (8CI, 9CI) (CA INDEX NAME)

$$\begin{array}{c} D \\ D \\ D \\ \end{array}$$

RN 1516-08-1 HCA

CN Ethanol-d6 (9CI) (CA INDEX NAME)

D3C-CD2-O-D

RN 1665-00-5 HCA

CN Methane-d2, dichloro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 1693-74-9 HCA

CN Furan-d4, tetrahydro-d4- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$$D \longrightarrow D$$

RN 1735-17-7 HCA

CN Cyclohexane-d12 (6CI, 8CI, 9CI) (CA INDEX NAME)

RN 2037-26-5 HCA

CN Benzene-d5, methyl-d3- (9CI) (CA INDEX NAME)

RN 2206-27-1 HCA

CN Methane-d3, sulfinylbis- (9CI) (CA INDEX NAME)

RN 2679-89-2 HCA

CN Ethane-d5, 2,2'-oxybis- (9CI) (CA INDEX NAME)

 $D_3C-CD_2-O-CD_2-CD_3$

RN 4472-41-7 HCA

CN Formamide-1-d, N,N-di(methyl-d3)- (7CI, 8CI, 9CI) (CA INDEX NAME)

RN 7291-22-7 HCA

CN Pyridine-d5 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$$D \longrightarrow D \\ D \longrightarrow D$$

RN 7789-20-0 HCA

CN Water-d2 (9CI) (CA INDEX NAME)

D- O- D

RN 17222-37-6 HCA

CN Methane-d3, oxybis- (9CI) (CA INDEX NAME)

D3C-0-CD3

IC ICM C07K014-00

CC 7-2 (Enzymes)

Section cross-reference(s): 1, 3, 6, 10

essential protein pathogenic bacteria therapeutic target; sequence essential protein gene pathogenic bacteria; mass spectrometry essential protein pathogenic

bacteria; NMR spectrometry essential protein pathogenic bacteria; xray crystallog essential protein pathogenic bacteria; cloning essential protein pathogenic bacteria Molecular chaperones IT(60-kilodalton, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in cellular metab. and their use as antimicrobial targets) ΙΤ Enzymes, biological studies (DNA gyrases, subunit B; cloning and phys. characterization of microbial polypeptides involved in cellular metab. and their use as antimicrobial targets) ΙT Molecular chaperones (DnaK, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in cellular metab. and their use as antimicrobial targets) ΙT Proteins (GrpE, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in cellular metab. and their use as antimicrobial targets) ΙΤ Antibacterial agents Cryoprotectants Crystallization DNA sequences Drug design Drug screening Drug targets Enterococcus faecalis Epitopes Escherichia coli Haemophilus influenzae Mass spectrometry Molecular cloning NMR spectroscopy Pathogenic bacteria Protein sequences Pseudomonas aeruginosa Staphylococcus aureus Streptococcus pneumoniae (cloning and phys. characterization of microbial polypeptides involved in cellular metab. and their use as antimicrobial targets) ITHydrocarbon oils Polyoxyalkylenes, uses (cryoprotectant; cloning and phys. characterization of microbial polypeptides involved in cellular metab. and their use as antimicrobial targets)

ΙΤ

Solvents

(deuterium lock, for NMR spectroscopy; cloning and
phys. characterization of microbial polypeptides
involved in cellular metab. and their use as antimicrobial
targets)
Fusion proteins (chimeric proteins)
 (for improved soly. or stability; cloning and phys.
 characterization of microbial polypeptides involved in
 cellular metab. and their use as antimicrobial targets)

IT Flagellins

ΙΤ

(gene flic, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in cellular metab. and their use as antimicrobial targets)

(heavy, for mass spectrometry; cloning and

phys. characterization of microbial polypeptides involved in cellular metab. and their use as antimicrobial targets)

IT Proteins

(in cellular metab.; cloning and phys. characterization of microbial **polypeptides** involved in cellular metab. and their use as antimicrobial targets)

IT Molecular association

(protein-protein; cloning and phys. characterization of microbial polypeptides involved in cellular metab. and their use as antimicrobial targets)

IT Metabolism, microbial

(proteins involved in; cloning and phys. characterization of microbial polypeptides involved in cellular metab. and their use as antimicrobial targets)

IT Crystallography

(x-ray; cloning and phys. characterization of microbial polypeptides involved in cellular metab. and their use as antimicrobial targets)

TT 7440-23-5, Sodium-23, uses 7723-14-0, Phosphorus-31, uses 7727-37-9, Nitrogen-14, uses **7782-39-0**, Hydrogen-2, uses 7782-41-4, Fluorine-19, uses 10028-17-8, Hydrogen-3, uses 12184-88-2, Hydride 14390-96-6, Nitrogen-15, uses 14762-74-4, Carbon-13, uses

(NMR isotope; cloning and phys. characterization of microbial polypeptides involved in cellular metab. and their use as antimicrobial targets)

IT 612853-91-5P 612853-93-7P 612853-95-9P 612853-97-1P 612854-00-9P 612854-02-1P 612854-04-3P 612854-06-5P 612854-08-7P 612854-11-2P 612854-13-4P 612854-15-6P 612854-17-8P 612854-19-0P 612854-21-4P 612854-23-6P 612854-26-9P 612854-28-1P

(amino acid sequence; cloning and phys. characterization of microbial polypeptides involved in cellular metab. and

their use as antimicrobial targets) 9000-83-3, ATPase ΙT (cation-transporting, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in cellular metab. and their use as antimicrobial 9024-20-8P, Ribulose phosphate 3-epimerase 9024-82-2P, Inorg. ΙT 9026-37-3P, FAD synthetase 9026-99-7P, pyrophosphatase Phosphopantetheine adenylyltransferase 9031-92-9P, Phosphoglucosamine mutase 9032-82-0P, Riboflavin kinase 9075-71-2P, Biotin carboxylase (cloning and phys. characterization of microbial polypeptides involved in cellular metab. and their use as antimicrobial targets) 56-81-5, Glycerol, uses 64-18-6, Formic acid, uses 67-63-0, ΙΤ Isopropanol, uses 77-92-9, Citric acid, uses 107-21-1, Ethylene glycol, uses 5683-44-3, 3-Methyl-2,4-pentanediol 25322-68-3, Polyethylene glycol (cryoprotectant; cloning and phys. characterization of microbial polypeptides involved in cellular metab. and their use as antimicrobial targets) ΙT 666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3,

666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3, Methanol-d4 865-49-6, Chloroform-d 917-96-4, Methyl-d3 isocyanide 1076-43-3, Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9, Tetrahydrofuran-d8 1735-17-7, Cyclohexane-d12 2037-26-5 2206-27-1, Dimethyl sulfoxide-d6 2679-89-2, Diethyl-d10 ether 4472-41-7, N,N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Deuterium oxide 17222-37-6, Dimethyl-d6 ether

(deuterium lock solvent for NMR spectroscopy; cloning and phys. characterization of microbial polypeptides involved in cellular metab. and their use as antimicrobial targets)

ΙT 7429-91-6, Dysprosium, uses 7439-88-5, Iridium, uses Krypton, uses 7439-91-0, Lanthanum, uses 7439-92-1, Lead, uses 7439-94-3, Lutetium, uses 7439-97-6, Mercury, uses 7439-98-7, Molybdenum, uses 7440-00-8, Neodymium, uses 7440-04-2, Osmium, 7440-05-3, Palladium, uses 7440-06-4, Platinum, uses uses 7440-10-0, Praseodymium, uses 7440-15-5, Rhenium, uses 7440-16-6, Rhodium, uses 7440-18-8, Ruthenium, uses 7440-19-9, Samarium, uses 7440-22-4, Silver, uses 7440-24-6, Strontium, 7440-27-9, Terbium, uses 7440-25-7, Tantalum, uses 7440-28-0, Thallium, uses 7440-29-1, Thorium, uses 7440-30-4, Thulium, uses 7440-31-5, Tin, uses 7440-33-7, Tungsten, uses 7440-39-3, Barium, uses 7440-43-9, Cadmium, uses 7440-45-1, Cerium, uses 7440-48-4, Cobalt, uses 7440-52-0, Erbium, uses

ΙΤ

ΙΤ

ΙT

ΤT

ΙT

612839-18-6

```
7440-53-1, Europium, uses
                            7440-54-2, Gadolinium, uses 7440-57-5,
Gold, uses
            7440-60-0, Holmium, uses 7440-61-1, Uranium, uses
7440-63-3, Xenon, uses 7440-64-4, Ytterbium, uses
                                                      7553-56-2,
              7726-95-6, Bromine, uses 7782-49-2, Selenium, uses
Iodine, uses
   (heavy atom for mass spectrometry; cloning
   and phys. characterization of microbial polypeptides
   involved in cellular metab. and their use as antimicrobial
   targets)
59-67-6D, Nicotinic acid, derivs. 621-82-9D, Cinnamic acid,
derivs.
   (mass spectrometry of; cloning and phys.
   characterization of microbial polypeptides involved in
   cellular metab. and their use as antimicrobial targets)
612853-90-4, DNA (Staphylococcus aureus gene rpe)
                                                      612853-92-6, DNA
(Escherichia coli gene rpe) 612853-94-8, DNA (Escherichia coli
            612853-96-0, DNA (Staphylococcus aureus gene accD)
612853-98-2, DNA (Staphylococcus aureus gene accD)
                                                       612853-99-3,
DNA (Streptococcus pneumoniae gene gyrB)
                                           612854-01-0, DNA
(Streptococcus pneumoniae gene gyrB) 612854-03-2, DNA
(Staphylococcus aureus gene accC)
                                   612854-05-4, DNA (Staphylococcus
aureus gene accC)
                    612854-07-6, DNA (Pseudomonas aeruginosa gene
        612854-09-8, DNA (Pseudomonas aeruginosa gene accC)
accC)
612854-10-1, DNA (Pseudomonas aeruginosa gene rpe)
                                                       612854-12-3,
DNA (Pseudomonas aeruginosa gene rpe)
                                        612854-14-5, DNA
(Streptococcus pneumoniae gene ribC) 612854-16-7, DNA (Streptococcus pneumoniae gene kdtB) 612854-20-3, DNA (Streptococcus pneumoniae gene kdtB) 612854-22-5, DNA (Haemophilus
influenzae gene IPYR) 612854-24-7, DNA (Haemophilus influenzae
             612854-25-8, DNA (Pseudomonas aeruginosa gene MRSA)
gene IPYR)
612854-27-0, DNA (Pseudomonas aeruginosa gene MRSA)
   (nucleotide sequence; cloning and phys. characterization of
   microbial polypeptides involved in cellular metab. and
   their use as antimicrobial targets)
3211-76-5, Selenomethionine
   (protein label for mass spectrometry; cloning
   and phys. characterization of microbial polypeptides
   involved in cellular metab. and their use as antimicrobial
   targets)
9014-08-8, Enolase 9023-46-5, Threonyl-tRNA synthetase
71822-24-7, Malate:quinone oxidoreductase
   (protein-protein interactions of; cloning and phys.
   characterization of microbial polypeptides involved in
   cellular metab, and their use as antimicrobial targets)
612838-99-0
              612839-00-6
                            612839-01-7
                                           612839-02-8
                                                          612839-03-9
612839-04-0
              612839-05-1 612839-06-2 612839-07-3
                                                          612839-08-4
612839-09-5 612839-10-8 612839-11-9 612839-12-0
                                                          612839-13-1
```

612839-14-2 612839-15-3 612839-16-4 612839-17-5

```
612839-19-7
              612839-20-0
                            612839-21-1
                                          612839-22-2
                                                         612839-23-3
612839-24-4
              612839-25-5
                            612839-26-6
                                          612839-27-7
                                                         612839-28-8
612839-29-9
              612866-32-7
                            612866-33-8
                                          612866-34-9
                                                         612866-35-0
612866-36-1
              612866-37-2
                            612866-38-3
                                          612866-39-4
                                                         612866-40-7
612866-41-8
              612866-42-9
                            612866-43-0
                                          612866-44-1
                                                         612866-45-2
612866-46-3
              612866-47-4
                            612866-48-5
                                          612866-49-6
                                                         612866-50-9
612866-51-0
              612866-52-1
                            612866-53-2
                                          612866-54-3
                                                         612866-55-4
   (unclaimed sequence; cloning and phys. characterization of
  microbial polypeptides involved in cellular metab. and
   their use as antimicrobial targets)
```

ΙT 9023-93-2P, Acetyl-CoA carboxylase

> (.beta.-subunit; cloning and phys. characterization of microbial polypeptides involved in cellular metab. and their use as antimicrobial targets)

L101 ANSWER 9 OF 28 HCA COPYRIGHT 2004 ACS on STN 139:319340 Cloning and physical characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets. Edwards, Aled; Dharamsi, Akil; Vedadi, Masoud; Alam, Muhammad Zahoor; Arrowsmith, Cheryl; Awrey, Donald; Beattie, Bryan; Richards, Dawn; Canadien, Veronica; Domagala, Megan; Houston, Simon; Mansoury, Kamran; Li, Qin; Nethery, Kathleen; Virag, Cristina; Ng, Ivy; Ouyang, Hui; Tai, Matthew; Thalakada, Rosanne; Kanagarajah, Dhushy (Affinium Pharmaceuticals, Inc., Can.; et al.). PCT Int. Appl. WO 2003083099 A2 20031009, 369 DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-CA462 20030402. PRIORITY: US 2002-PV369511 20020402; US 2002-PV385089 20020531; US 2002-PV385751 20020604; US 2002-PV386553 20020605; US 2002-PV386577 20020605; US 2002-PV386367 20020605; US 2002-PV386566 20020605; US 2002-PV386390 20020606; US 2002-PV386601 20020606; US 2002-PV399972 20020731; US 2002-PV424053 20021105; US 2002-PV436834 20021227; US 2002-PV436804 20021227; US 2002-PV436861 20021227; US 2002-PV437281 20021231; US 2002-PV437527 20021231. AΒ The present invention relates to polypeptide targets for pathogenic bacteria. Reliable, high throughput methods are developed to identify, express, and purify a no. of antimicrobial targets from Staphylococcus aureus, Escherichia coli, Streptococcus pneumoniae, Enterococcus faecalis, Haemophilus influenzae, and Pseudomonas aeruginosa. The nucleic acid and amino acid sequences

are provided for O-sialoglycoprotein endopeptidase, glycyl-tRNA

ΙΤ

RN

CN

D- D

ΙΤ

RN

CN

RN

CN

RN

CN

synthetase .alpha.-subunit, translation elongation factor G, methionine aminopeptidase, phenylalanyl-tRNA synthetase .alpha.-subunit, peptide chain release factor RF-2, tRNA (quanine-7-) methyltransferase, and histidyl-tRNA synthetase. The invention also provides bioinformatic, biochem. and biophys. characteristics of those polypeptides, in particular characterization by mass spectrometry, NMR spectrometry, and x-ray crystallog. 7782-39-0, Hydrogen-2, uses (NMR isotope; cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets) 7782-39-0 HCA Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME) 666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3, Methanol-d4 865-49-6, Chloroform-d 917-96-4, Methyl-d3 isocyanide 1076-43-3, Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9 , Tetrahydrofuran-d8 1735-17-7, Cyclohexane-d12 2037-26-5 2206-27-1, Dimethyl sulfoxide-d6 2679-89-2, Diethyl-d10 ether 4472-41-7, N, N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Deuterium oxide 17222-37-6, Dimethyl-d6 ether (deuterium lock solvent for NMR spectroscopy; cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets) 666-52-4 HCA 2-Propanone-1,1,1,3,3,3-d6 (9CI) (CA INDEX NAME) D3C-C-CD3 811-98-3 HCA Methanol-d4 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME) D3C-0-D 865-49-6 HCA Methane-d, trichloro- (9CI) (CA INDEX NAME)

RN 917-96-4 HCA

CN Methane-d3, isocyano- (9CI) (CA INDEX NAME)

RN 1076-43-3 HCA

CN Benzene-d6 (8CI, 9CI) (CA INDEX NAME)

$$\begin{array}{c|c} D & D \\ \hline D & D \\ \hline D & D \\ \end{array}$$

RN 1516-08-1 HCA

CN Ethanol-d6 (9CI) (CA INDEX NAME)

RN 1665-00-5 HCA

CN Methane-d2, dichloro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 1693-74-9 HCA

CN Furan-d4, tetrahydro-d4- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$$D \longrightarrow D$$

RN 1735-17-7 HCA CN Cyclohexane-d12 (6CI, 8CI, 9CI) (CA INDEX NAME)

RN 2037-26-5 HCA

CN Benzene-d5, methyl-d3- (9CI) (CA INDEX NAME)

RN 2206-27-1 HCA

CN Methane-d3, sulfinylbis- (9CI) (CA INDEX NAME)

RN 2679-89-2 HCA

CN Ethane-d5, 2,2'-oxybis- (9CI) (CA INDEX NAME)

 $D_3C-CD_2-O-CD_2-CD_3$

RN 4472-41-7 HCA

CN Formamide-1-d, N, N-di(methyl-d3) - (7CI, 8CI, 9CI) (CA INDEX NAME)

RN 7291-22-7 HCA

CN Pyridine-d5 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$$\begin{array}{c|c} D & D \\ \hline \end{array}$$

RN 7789-20-0 HCA

CN Water-d2 (9CI) (CA INDEX NAME)

D- O- D

RN 17222-37-6 HCA

CN Methane-d3, oxybis- (9CI) (CA INDEX NAME)

D3C-0-CD3

IC ICM C12N009-10 ICS G06F017-50

CC 7-2 (Enzymes)

Section cross-reference(s): 1, 3, 6, 10

essential protein pathogenic bacteria therapeutic target; sequence essential protein gene pathogenic bacteria; mass spectrometry essential protein pathogenic bacteria; NMR spectrometry essential protein pathogenic bacteria; xray crystallog essential protein pathogenic bacteria; cloning essential protein pathogenic bacteria

IT Molecular chaperones
(DnaK, protein-protein interactions of; cloning and phys.
characterization of microbial polypeptides involved in
protein synthesis and modification and their use as antimicrobial

targets)

IT Elongation factors (protein formation)
(EF-G; cloning and phys. characterization of microbial polypeptides involved in protein synthesis and

modification and their use as antimicrobial targets) TΤ Ribosomal proteins (L6, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets) ΙT Termination factors (protein formation) (RF-2 (release factor 2); cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets) ΙT Ribosomal proteins (S2, protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets) Antibacterial agents ΙT Cryoprotectants Crystallization DNA sequences Drug design Drug screening Drug targets Enterococcus faecalis Epitopes Escherichia coli Haemophilus influenzae Mass spectrometry Molecular cloning NMR spectroscopy Pathogenic bacteria Protein sequences Pseudomonas aeruginosa Staphylococcus aureus Streptococcus pneumoniae (cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets) ΙT Hydrocarbon oils Polyoxyalkylenes, uses (cryoprotectant; cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets) ΙT Solvents (deuterium lock, for NMR spectroscopy; cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets) ITFusion proteins (chimeric proteins)

ΙT

ΙT

ΙT

ΙT

ΙΤ

ΙT

ΙΤ

(for improved soly. or stability; cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial Elements (heavy, for mass spectrometry; cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets) Proteins (in protein synthesis and modification; cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets) Flagellins (protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets) Molecular association (protein-protein; cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets) Crystallography (x-ray; cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets) 7723-14-0, Phosphorus-31, uses 7440-23-5, Sodium-23, uses 7727-37-9, Nitrogen-14, uses **7782-39-0**, Hydrogen-2, uses 7782-41-4, Fluorine-19, uses 10028-17-8, Hydrogen-3, uses 12184-88-2, Hydride 14390-96-6, Nitrogen-15, uses 14762-74-4, Carbon-13, uses (NMR isotope; cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets) 612099-25-9P 612099-27-1P 612099-21-5P 612099-23-7P 612099-33-9P 612099-35-1P 612099-29-3P 612099-31-7P 612099-41-9P 612099-37-3P 612099-39-5P 612099-43-1P 612099-50-0P 612099-52-2P 612099-46-4P 612099-48-6P 612099-58-8P 612099-54-4P 612099-60-2P 612099-56-6P 612099-62-4P 612099-64-6P 612099-70-4P 612099-67-9P 612099-7 612099-75-9P 612549-61-8P 612549-63-0P 3-7P (amino acid sequence; cloning and phys. characterization of

and modification and their use as antimicrobial targets)

IT 9037-62-1P, Glycyl-tRNA synthetase 9055-66-7P, Phenylalanyl-tRNA synthetase 9068-78-4P, Histidyl-tRNA synthetase 37257-00-4P, TRNA (guanine-7-)methyltransferase 39391-17-8P, TRNA

microbial polypeptides involved in protein synthesis

5-aminomethyl-2-thiouridylate 5'-methyltransferase 61229-81-0P, Methionine aminopeptidase 129430-53-1P, O-Sialoglycoprotein endopeptidase

(cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets) 56-81-5, Glycerol, uses 64-18-6, Formic acid, uses Isopropanol, uses 77-92-9, Citric acid, uses 107-21-1, Ethylene 5683-44-3, 3-Methyl-2,4-pentanediol glycol, uses 25322-68-3,

(cryoprotectant; cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets)

666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3, Methanol-d4 865-49-6, Chloroform-d 917-96-4, Methyl-d3 isocyanide 1076-43-3, Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9 , Tetrahydrofuran-d8 1735-17-7, Cyclohexane-d12 2037-26-5 2206-27-1, Dimethyl sulfoxide-d6 2679-89-2, Diethyl-d10 ether 4472-41-7, N, N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Deuterium oxide 17222-37-6, Dimethyl-d6 ether

ΙT

IT

Polyethylene glycol

(deuterium lock solvent for NMR spectroscopy; cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets)

7429-91-6, Dysprosium, uses 7439-88-5, Iridium, uses 7439-90-9, ΤТ Krypton, uses 7439-91-0, Lanthanum, uses 7439-92-1, Lead, uses 7439-94-3, Lutetium, uses 7439-97-6, Mercury, uses 7439-98-7, Molybdenum, uses 7440-00-8, Neodymium, uses 7440-04-2, Osmium, 7440-05-3, Palladium, uses 7440-06-4, Platinum, uses 7440-10-0, Praseodymium, uses 7440-15-5, Rhenium, uses 7440-16-6, Rhodium, uses 7440-18-8, Ruthenium, uses Samarium, uses 7440-22-4, Silver, uses 7440-24-6, Strontium, 7440-25-7, Tantalum, uses 7440-27-9, Terbium, uses 7440-28-0, Thallium, uses 7440-29-1, Thorium, uses 7440-30-4, Thulium, uses 7440-31-5, Tin, uses 7440-33-7, Tungsten, uses 7440-39-3, Barium, uses 7440-43-9, Cadmium, uses 7440-45-1, Cerium, uses 7440-48-4, Cobalt, uses 7440-52-0, Erbium, uses 7440-53-1, Europium, uses 7440-54-2, Gadolinium, uses 7440-57-5, Gold, uses 7440-60-0, Holmium, uses 7440-61-1, Uranium, uses 7440-63-3, Xenon, uses 7440-64-4, Ytterbium, uses 7553-56-2, Iodine, uses 7726-95-6, Bromine, uses 7782-49-2, Selenium, uses (heavy atom for mass spectrometry; cloning and phys. characterization of microbial polypeptides

involved in protein synthesis and modification and their use as antimicrobial targets)

IT 59-67-6D, Nicotinic acid, derivs. 621-82-9D, Cinnamic acid, derivs.

(mass spectrometry of; cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets)

612099-20-4, DNA (Staphylococcus aureus gene ycfB) IT 612099-22-6, DNA (Staphylococcus aureus gene ygiD) 612099-24-8, DNA (Staphylococcus aureus gene ygiD) 612099-26-0, DNA (Streptococcus 612099-28-2, DNA (Streptococcus pneumoniae pneumoniae gene glyQ) 612099-30-6, DNA (Streptococcus pneumoniae gene yrdC) gene glv0) 612099-34-0, 612099-32-8, DNA (Streptococcus pneumoniae gene yrdC) DNA (Enterococcus faecalis gene fusA) 612099-36-2, DNA (Enterococcus faecalis gene fusA) 612099-38-4, DNA (Pseudomonas aeruginosa gene ygjD) 612099-40-8, DNA (Pseudomonas aeruginosa 612099-42-0, DNA (Pseudomonas aeruginosa gene map) gene vgjD) 612099-44-2, DNA (Pseudomonas aeruginosa gene map) 612099-45-3, DNA (Streptococcus pneumoniae gene fusA) 612099-47-5, DNA 612099-49-7, DNA (Streptococcus pneumoniae gene fusA) (Enterococcus faecalis gene pheS) 612099-51-1, DNA (Enterococcus 612099-53-3, DNA (Escherichia coli gene prfB) faecalis gene pheS) 612099-55-5, DNA (Escherichia coli gene prfB) 612099-57-7, DNA 612099-59-9, DNA (Escherichia coli (Escherichia coli gene trmD) 612099-61-3, DNA (Enterococcus faecalis gene map) gene trmD) 612099-63-5, DNA (Enterococcus faecalis gene map) 612099-65-7, DNA 612099-66-8, DNA (Haemophilus (Haemophilus influenzae gene SYH) 612099-68-0, DNA (Haemophilus influenzae gene influenzae gene map) 612099-69-1, DNA (Staphylococcus aureus gene map) 612099-71-5, DNA (Staphylococcus aureus gene map) 612099-72-6, DNA (Streptococcus pneumoniae gene map) 612099-74-8, DNA (Streptococcus pneumoniae gene map) 612549-62-9, DNA (Haemophilus influenzae gene SYH)

(nucleotide sequence; cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets)

IT 3211-76-5, Selenomethionine

(protein label for mass spectrometry; cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets)

IT 9027-73-0, 5'-Nucleotidase 9075-65-4, Glycerol-3-phosphate dehydrogenase 394250-11-4, Oligopeptidase A (protein-protein interactions of; cloning and phys. characterization of microbial polypeptides involved in protein synthesis and modification and their use as antimicrobial targets)

IT 612100-55-7 612100-56-8 612100-57-9 612100-58-0 612100-60-4 612100-61-5 612100-62-6 612100-63-7 612100-64-8 612100-65-9

ΙT

ΙT

```
612100-68-2
                                               612100-69-3
                                                             612100-70-6
     612100-66-0
                   612100-67-1
                                               612100-75-1
     612100-71-7
                   612100-72-8
                                 612100-73-9
                                                             612100-76-2
     612100-77-3
                   612100-78-4
                                 612100-79-5
                                               612100-80-8
                                                             612100-81-9
     612100-82-0
                   612100-83-1
                                 612100-84-2
                                               612100-85-3
                                                             612100-86-4
     612100-87-5
                   612100-88-6
        (unclaimed nucleotide sequence; cloning and phys.
        characterization of microbial polypeptides involved in
        protein synthesis and modification and their use as antimicrobial
        targets)
     612100-74-0
        (unclaimed protein sequence; cloning and phys. characterization
        of microbial polypeptides involved in protein synthesis
        and modification and their use as antimicrobial targets)
                   612077-66-4
                                                             612077-72-2
     612077-64-2
                                 612077-68-6
                                               612077-70-0
     612077-74-4
                   612077-76-6
                                 612077-78-8
                                               612077-80-2
                                                             612077-82-4
                   612077-86-8
                                 612077-88-0
                                               612077-90-4
                                                             612077-92-6
     612077-84-6
     612077-95-9
                   612077-97-1
                                 612077-99-3
                                               612078-01-0
                                                             612078-02-1
                                 612078-07-6
                                               612078-09-8
                                                             612078-11-2
     612078-03-2 612078-05-4
     612078-15-6
                   612078-17-8
                                612078-19-0
                                               612078-21-4
                                                             612078-23-6
     612078-25-8
                  612078-27-0 612078-29-2 612078-31-6
                                                             612078-33-8
                                 612078-39-4
                                              612078-41-8
                                                             612078-43-0
     612078-35-0
                   612078-37-2
                                               612078-50-9
                                                             612078-52-1
                   612078-46-3
                                 612078-48-5
     612078-45-2
     612100-59-1
        (unclaimed sequence; cloning and phys. characterization of
        microbial polypeptides involved in protein synthesis
        and modification and their use as antimicrobial targets)
L101 ANSWER 10 OF 28 HCA COPYRIGHT 2004 ACS on STN
            Isolation and isotope labeling of cysteine
139:210352
     - and methionine-containing tryptic peptides: Application
     to the study of cell surface proteolysis. Shen, Min; Guo, Lin;
    Wallace, Alison; Fitzner, Jeff; Eisenman, June; Jacobson, Erik;
     Johnson, Richard S. (Amgen Corporation, Seattle, WA, 98101-2936,
     USA). Molecular and Cellular Proteomics, 2(5), 315-324 (English)
                           ISSN: 1535-9476. Publisher: American Society
     2003.
           CODEN: MCPOBS.
     for Biochemistry and Molecular Biology.
AΒ
     Inexpensive methods were developed for isolating and
     isotopically labeling tryptic peptides that
     contain either cysteine or methionine.
                                           After covalently
     capturing cysteine-contg. peptides with pyridyl
     disulfide reactive groups on agarose beads, extensive wash
     steps were applied, and the attached peptides were
     released using a reducing agent. This approach results in less
     nonspecifically bound peptides and eliminates the
     possibility of generating avidin peptide background ions
     that can arise when using methods based on biotin and avidin (e.g.
     isotope-coded affinity tag). The thiols were alkylated
     using either N-ethyl- or N-D5-ethyl-iodoacetamide, both of which can
```

be synthesized in a single step using inexpensive reagents. This isotopic labeling does not greatly increase the peptide mass, nor does it affect the peptide ion charge state in electrospray ionization. In addn., methionine-contg. peptides were captured using com. available methionine-reactive beads, and relative quantitation of peptides was achieved by isotopic labeling of amino groups using activated esters of either nicotinic acid or D4-nicotinic acid. These methods were used to study the metalloprotease-mediated shedding of cell surface proteins from a mouse monocyte cell line that had been treated with a phorbol ester and lipopolysaccharide. In addn. to the identification of proteins previously detd. to be inducibly shed, three new shed proteins were identified: CD18, ICOS ligand, and tumor endothelial marker 7-related protein.

CC 9-16 (Biochemical Methods)

ST isolation isotope labeling cell surface protein detn

IT Cell membrane

Protein degradation

(isolation and **isotope** labeling of **cysteine**and methionine-contg. tryptic **peptides** for detn of cell surface proteins)

IT Peptides, analysis

Proteins

(isolation and **isotope** labeling of **cysteine**and methionine-contg. tryptic **peptides** for detn of cell surface proteins)

IT Integrins

(.beta.2; isolation and **isotope** labeling of **cysteine**— and methionine—contg. tryptic **peptides** for detn of cell surface proteins)

L101 ANSWER 11; OF 28 HCA COPYRIGHT 2004 ACS on STN
139:18838 Bacterial polypeptides involved in general
metabolism and their characterization as antimicrobial targets.
Edwards, Aled; Dharamsi, Akil; Vedadi, Masoud; Alam, Muhammad
Zahoor; Awrey, Donald; Beattie, Bryan; Canadien, Veronica; Domagala,
Megan; Houston, Simon; Li, Qin; Mansoury, Kamran; Necakov, Sasha;
Nethery, Kathleen; Ouyang, Hui; Pinder, Benjamin; Sheldrick, Bay;
Vallee, Francois; Wrezel, Olga (Affinium Pharmaceuticals, Inc.,
Can.; et al.). PCT Int. Appl. WO 2003045986 A2 20030605, 272 pp.
DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR,
BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ,
OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR,
TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ,

AB

IT

RN

CN

```
MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK,
ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN,
TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-CA1785
20021126. PRIORITY: US 2001-PV333340 20011126; US 2001-PV333414
20011126; US 2001-PV333423 20011126; US 2001-PV333419 20011126; US
2001-PV333342 20011126; US 2001-PV341951 20011219; US 2001-PV342558
20011220; US 2001-PV342557 20011220; US 2001-PV343613 20011228; US
2001-PV344272 20011228.
The present invention relates to ten polypeptide targets
for pathogenic bacteria. The invention also provides biochem. and
biophys. characteristics of those polypeptides. Reliable,
high throughput methods are developed to identified, express, and
purify a no. of antimicrobial targets from Escherichia coli,
Staphylococcus aureus, Helicobacter pylori, Staphylococcus
pneumoniae, and Pseudomonas aeruginosa. The invention provides the
nucleic acid and amino acid sequences of glucose-inhibited division
protein from E. coli, fructose bisphosphate aldolase from S. aureus,
replicative DNA helicase primosome component from H. pylori, protein
factor essential for expression of methicillin resistance from S.
aureus, glucosamine-fructose-6-phosphate aminotransferase from S.
aureus, N utilization substance protein B from S. pneumoniae, N
utilization substance protein A from P. aeruginosa, putative
GTP-binding protein from G. aeruginosa, 2-dehydro-3-
deoxyphosphooctonate aldolase from P. aeruginosa, and putative
GTP-binding protein in thiophene and furan oxidn. from S. aureus.
The invention also provides purified, sol. forms of
polypeptides suitable for structural and functional
 characterization using a variety of techniques, including, for
 example, affinity chromatog., mass spectrometry,
 NMR, and x-ray crystallog. The invention further provides modified
 versions of the polypeptides to facilitate
 characterization, including polypeptides labeled with
 isotopic or heavy atoms and fusion proteins. One or more
 crystd. forms of the polypeptides may also be provided.
 666-52-4, 2-Propanone-1, 1, 1, 3, 3, 3-d6 811-98-3,
 Methanol-d4 865-49-6, Deutero-chloroform 1076-43-3
 , Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5
 1693-74-9, Tetrahydrofuran-d8 2037-26-5
 2206-26-0, Acetonitrile-d3 2206-27-1
 2679-89-2, Diethyl ether-d10 4472-41-7,
 N, N-Dimethylformamide-d7 7291-22-7, Pyridine-d5
 7789-20-0, Deuterium oxide 17222-37-6
    (NMR deuterium lock solvent; bacterial
    polypeptides involved in general metab. and their
    characterization as antimicrobial targets)
  666-52-4
          HCA
 2-Propanone-1,1,1,3,3,3-d6 (9CI) (CA INDEX NAME)
```

RN 811-98-3 HCA

CN Methanol-d4 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

D3C-0-D

RN 865-49-6 HCA

CN Methane-d, trichloro- (9CI) (CA INDEX NAME)

RN 1076-43-3 HCA

CN Benzene-d6 (8CI, 9CI) (CA INDEX NAME)

$$\begin{array}{c|c} D & D \\ \hline D & D \\ \hline \end{array}$$

RN 1516-08-1 HCA

CN Ethanol-d6 (9CI) (CA INDEX NAME)

D3C-CD2-O-D

RN 1665-00-5 HCA

CN Methane-d2, dichloro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 1693-74-9 HCA

CN Furan-d4, tetrahydro-d4- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$$D \qquad D \qquad D$$

RN 2037-26-5 HCA

CN Benzene-d5, methyl-d3- (9CI) (CA INDEX NAME)

RN 2206-26-0 HCA

CN Acetonitrile-d3 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 2206-27-1 HCA

CN Methane-d3, sulfinylbis- (9CI) (CA INDEX NAME)

RN 2679-89-2 HCA

CN Ethane-d5, 2,2'-oxybis- (9CI) (CA INDEX NAME)

D₃C-CD₂-O-CD₂-CD₃

RN 4472-41-7 HCA

CN Formamide-1-d, N, N-di(methyl-d3) - (7CI, 8CI, 9CI) (CA INDEX NAME)

RN 7291-22-7 HCA

CN Pyridine-d5 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 7789-20-0 HCA

CN Water-d2 (9CI) (CA INDEX NAME)

D- O- D

RN 17222-37-6 HCA

CN Methane-d3, oxybis- (9CI) (CA INDEX NAME)

D3C- O- CD3

IT 7782-39-0, Hydrogen-2, analysis

(NMR isotope label; bacterial polypeptides

involved in general metab. and their characterization as

antimicrobial targets)

RN 7782-39-0 HCA

```
Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME)
CN
D-D
     ICM C07K014-195
IC
     6-3 (General Biochemistry)
CC
     Section cross-reference(s): 1, 3, 7, 9, 10
     protein gene metab bacteria antimicrobial target; mass
ST
     spectrometry protein antimicrobial target; NMR
     spectrometry protein antimicrobial target; x ray
     crystallog protein antimicrobial target
     Enzymes, biological studies
ΙT
        (DNA helicase; bacterial polypeptides involved in
        general metab. and their characterization as antimicrobial
        targets)
ΙΤ
     Proteins
        (GTP-binding; bacterial polypeptides involved in
        general metab. and their characterization as antimicrobial
        targets)
ΙT
     Proteins
        (Gene femA (Methicillin resistance protein); bacterial
        polypeptides involved in general metab. and their
        characterization as antimicrobial targets)
ΙT
     Proteins
        (Gene trmE (GTP-binding protein in thiophene and furan oxidn.);
        bacterial polypeptides involved in general metab. and
        their characterization as antimicrobial targets)
ΙT
     Proteins
        (GidB (glucose-inhibited division protein B); bacterial
        polypeptides involved in general metab. and their
        characterization as antimicrobial targets)
ΙΤ
     Gene, microbial
        (KD08PS; bacterial polypeptides involved in general
        metab. and their characterization as antimicrobial targets)
     Affinity chromatography
ΙT
     Antimicrobial agents
     Bacteria (Eubacteria)
     Cryoprotectants
     Crystallization
     Drug design
     Drug targets
     Epitopes
     Escherichia coli
     Helicobacter pylori
       Mass spectrometry
     Molecular cloning
     NMR spectroscopy
```

ΙT

ΙT

ΙΤ

ΙT

ΙΤ

ΙT

ΙΤ

ΙT

ΙT

ΙT

IT

ΙΤ

ΙT

ΙT

Pseudomonas aeruginosa Staphylococcus aureus Streptococcus pneumoniae (bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) Proteins (bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) Fusion proteins (chimeric proteins) (bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) Hydrocarbon oils Polyoxyalkylenes, analysis (cryoprotectant; bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) Gene, microbial (dnaB gene; bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) DNA formation factors (dnaB; bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) Gene, microbial (fbaA; bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) Gene, microbial (femA; bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) Gene, microbial (gidB; bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) Gene, microbial (glmS; bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) Transcription factors (nusA (N utilization substance A); bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) Gene, microbial (nusA; bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) Transcription factors (nusB; bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) Gene, microbial (nusB; bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) Conformation

(three-dimensional structure; bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) ΙT Gene, microbial (trmE; bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) ΙT Crystallography (x-ray; bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) Gene, microbial ΙΤ (ychF; bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) 110-82-7, Cyclohexane, analysis 666-52-4, ΙT 2-Propanone-1,1,1,3,3,3-d6 811-98-3, Methanol-d4 865-49-6, Deutero-chloroform 1076-43-3, Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9 , Tetrahydrofuran-d8 2037-26-5 2206-26-0, Acetonitrile-d3 2206-27-1 2679-89-2, Diethyl ether-d10 4472-41-7, N,N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Deuterium oxide 17222-37-6 (NMR deuterium lock solvent; bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) 7440-23-5, Sodium-23, analysis 7723-14-0, Phosphorus-31, analysis TΤ 7727-37-9, Nitrogen-14, analysis 7782-39-0, Hydrogen-2, analysis 7782-41-4, Fluorine-19, analysis 10028-17-8, Hydrogen-3, analysis 12184-88-2, Hydride 14390-96-6, Nitrogen-15, analysis 14762-74-4, Carbon-13, analysis (NMR isotope label; bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) 538409-36-8P, Protein (Escherichia coli gene gidB) 538409-37-9P, ΙT Protein (Escherichia coli gene gidB) 538409-39-1P 538409-41-5P 538409-43-7P 538409-45-9P 538409-47-1P 538409-48-2P 538409-54**-**0P 538409-56-2P 538409-50-6P 538409-52-8P 538409-58-4P 538409-61-9P 538409-63-1P 538409-67-5P 538409-69-7P 538409-70-0P 538409-65-3P (amino acid sequence; bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) 9024-52-6P, Fructose bisphosphate aldolase 9026-96-4P, ΙT 2-Keto-3-deoxy-8-phosphooctonic synthetase 9030-45-9P, Glucosamine-fructose-6-phosphate aminotransferase (bacterial polypeptides involved in general metab. and their characterization as antimicrobial targets) TΤ 56-81-5, Glycerol, analysis 64-18-6, Formic acid, analysis 67-63-0, Isopropanol, analysis 77-92-9, Citric acid, analysis

```
107-41-5, 2-Methvl
    107-21-1, Ethylene glycol, analysis
                       25322-68-3, Polyethylene glycol
    2,4-pentanediol
        (cryoprotectant; bacterial polypeptides involved in
       general metab. and their characterization as antimicrobial
        targets)
                                   7429-91-6, Dysprosium, analysis
ΙT
    3211-76-5, Selenomethionine
     7439-88-5, Iridium, analysis
                                    7439-90-9, Krypton, analysis
                                      7439-92-1, Lead, analysis
    7439-91-0, Lanthanum, analysis
                                     7439-97-6, Mercury, analysis
    7439-94-3, Lutetium, analysis
    7439-98-7, Molybdenum, analysis
                                      7440-00-8, Neodymium, analysis
                                   7440-05-3, Palladium, analysis
    7440-04-2, Osmium, analysis
                                     7440-10-0, Praseodymium, analysis
    7440-06-4, Platinum, analysis
    7440-15-5, Rhenium, analysis
                                    7440-16-6, Rhodium, analysis
                                      7440-19-9, Samarium, analysis
    7440-18-8, Ruthenium, analysis
                                  7440-24-6, Strontium, analysis
    7440-22-4, Silver, analysis
                                    7440-27-9, Terbium, analysis
    7440-25-7, Tantalum, analysis
                                    7440-29-1, Thorium, analysis
    7440-28-0, Thallium, analysis
                                   7440-31-5, Tin, analysis 7440-33-7,
    7440-30-4, Thulium, analysis
    Tungsten, analysis 7440-39-3, Barium, analysis 7440-43-9,
                                                      7440-48-4, Cobalt,
    Cadmium, analysis
                         7440-45-1, Cerium, analysis
                                             7440-53-1, Europium,
               7440-52-0, Erbium, analysis
    analysis
                                                  7440-57-5, Gold,
               7440-54-2, Gadolinium, analysis
    analysis
               7440-60-0, Holmium, analysis 7440-61-1, Uranium,
    analysis
                                            7440-64-4, Ytterbium,
               7440-63-3, Xenon, analysis
    analysis
                                             7726-95-6, Bromine,
               7553-56-2, Iodine, analysis
    analvsis
               7782-49-2, Selenium, analysis
    analysis
        (label suitable for mass spectrometry;
       bacterial polypeptides involved in general metab. and
        their characterization as antimicrobial targets)
     59-67-6D, Nicotinic acid, protein derivs.
                                                 621-82-9D, Cinnamic
ΙT
     acid, protein derivs.
        (matrix suitable for mass spectrometry;
        bacterial polypeptides involved in general metab. and
        their characterization as antimicrobial targets)
                                                   538409-38-0, DNA
     538409-35-7, DNA (Escherichia coli gene gidB)
ΙΤ
                                        538409-40-4, DNA (Staphylococcus
     (Staphylococcus aureus gene fbaA)
                         538409-42-6, DNA (Helicobacter pylori gene dnaB)
     aureus gene fbaA)
     538409-44-8, DNA (Helicobacter pylori gene dnaB)
                                                        538409-46-0, DNA
     (Staphylococcus aureus gene femA)
                                         538409-49-3, DNA (Staphylococcus
                         538409-51-7, DNA (Staphylococcus aureus gene
     aureus gene glmS)
                                        538409-57-3, DNA (Pseudomonas
             538409-53-9
                           538409-55-1
                            538409-59-5, DNA (Pseudomonas aeruginosa
     aeruginosa gene nusA)
                  538409-60-8, DNA (Pseudomonas aeruginosa gene ychF)
     gene nusA)
     538409-62-0, DNA (Pseudomonas aeruginosa gene ychF)
                                                           538409-64-2,
     DNA (Pseudomonas aeruginosa gene DK08PS)
                                                538409-66-4, DNA
     (Pseudomonas aeruginosa gene DK08PS) 538409-68-6, DNA
     (Staphylococcus aureus gene trmE)
        (nucleotide sequence; bacterial polypeptides involved
```

```
in general metab. and their characterization as antimicrobial
        targets)
                   538419-20-4
                                 538419-33-9
                                               538419-34-0
                                                             538419-46-4
IT
     538419-19-1
                                                             538419-71-5
                   538419-54-4
                                 538419-55-5
                                               538419-70-4
     538419-47-5
                                 538419-91-9
                                               538419-93-1
                                                              538420-02-9
                   538419-82-8
     538419-81-7
                   538420-11-0
                                 538420-13-2
                                               538420-21-2
                                                              538420-22-3
     538420-03-0
        (unclaimed nucleotide sequence; bacterial polypeptides
        involved in general metab. and their characterization as
        antimicrobial targets)
                   503534-87-0
                                 503534-88-1
                                               538366-78-8
                                                              538366-80-2
     356063-59-7
IT
                                               538366-88-0
                                                             538366-90-4
                   538366-84-6
                                 538366-86-8
     538366-82-4
                                               538366-95-9
                                                             538366-96-0
     538366-92-6
                   538366-93-7
                                 538366-94-8
                                 538367-00-9
                                               538367-01-0
                                                             538367-02-1
     538366-97-1
                   538366-98-2
                                 538367-05-4
                                               538367-06-5
                                                             538367-07-6
                   538367-04-3
     538367-03-2
                                               538367-11-2
                                                             538367-12-3
     538367-08-7
                   538367-09-8
                                 538367-10-1
                                 538419-74-8
                   538419-64-6
     538367-13-4
        (unclaimed sequence; bacterial polypeptides involved in
        general metab. and their characterization as antimicrobial
        targets)
L101 ANSWER 12 OF 28 HCA COPYRIGHT 2004 ACS on STN
139:18837 Bacterial polypeptides involved in carbohydrate and
     coenzyme metabolism and their characterization as antimicrobial
               Edwards, Aled; Dharamsi, Akil; Vedadi, Masoud; Ng, Ivy;
     Alam, Muhammad Zahoor; Awrey, Donald; Beattie, Bryan; Domagala,
     Megan; Mansoury, Kamran; Pinder, Benjamin (Affinium Pharmaceuticals,
     Inc., Can.). PCT Int. Appl. WO 2003045985 A2 20030605, 191 pp.
     DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR,
     BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI,
     GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,
     LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ,
     OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR,
     TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ,
     MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK,
     ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN,
                 (English). CODEN: PIXXD2. APPLICATION: WO 2002-CA1784
     TD, TG, TR.
     20021126. PRIORITY: US 2001-PV333349 20011126; US 2001-PV333420
     20011126; US 2001-PV341950 20011219; US 2001-PV343643 20011228.
     The present invention relates to ten polypeptide targets
AΒ
     for pathogenic bacteria. The invention also provides biochem. and
     biophys. characteristics of those polypeptides. Reliable,
     high throughput methods are developed to identified, express, and
     purify a no. of antimicrobial targets from Escherichia coli,
     Staphylococcus aureus, and Pseudomonas aeruginosa. The invention
     provides the nucleic acid and amino acid sequences of
     phosphoglycerate kinase from S. aureus, flavoprotein affectin
     synthesis of DNA and pantothenate from E. coli, riboflavin
```

kinase/FAD synthase from S. aureus, and phosphopantetheine

adenylyltransferase from P. aeruginosa. The invention also provides purified, sol. forms of polypeptides suitable for structural and functional characterization using a variety of techniques, including, for example, affinity chromatog., mass spectrometry, NMR, and x-ray crystallog. The invention further provides modified versions of the polypeptides to facilitate characterization, including polypeptides labeled with isotopic or heavy atoms and fusion proteins. One or more crystd. forms of the polypeptides may also be provided. 666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3, ΙT Methanol-d4 865-49-6, Deutero-chloroform 1076-43-3 , Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9, Tetrahydrofuran-d8 2037-26-5 2206-26-0, Acetonitrile-d3 2206-27-1 2679-89-2, Diethyl ether-d10 4472-41-7, N, N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Deuterium oxide 17222-37-6 (NMR deuterium lock solvent; bacterial polypeptides involved in carbohydrate and coenzyme metab. and their characterization as antimicrobial targets) 666-52-4 RN CN2-Propanone-1,1,1,3,3,3-d6 (9CI) (CA INDEX NAME) RN 811-98-3 HCA Methanol-d4 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME) CND3C-0-D RN 865-49-6 HCA CN Methane-d, trichloro- (9CI) (CA INDEX NAME) Ď C1-C-C1 Cl

RN

CN

1076-43-3 HCA

Benzene-d6 (8CI, 9CI) (CA INDEX NAME)

$$\begin{array}{c} D \\ D \\ D \end{array}$$

RN 1516-08-1 HCA

CN Ethanol-d6 (9CI) (CA INDEX NAME)

D3C-CD2-O-D

RN 1665-00-5 HCA

CN Methane-d2, dichloro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 1693-74-9 HCA

CN Furan-d4, tetrahydro-d4- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$$D \qquad D \qquad D$$

RN 2037-26-5 HCA

CN Benzene-d5, methyl-d3- (9CI) (CA INDEX NAME)

RN 2206-26-0 HCA

CN Acetonitrile-d3 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 2206-27-1 HCA

CN Methane-d3, sulfinylbis- (9CI) (CA INDEX NAME)

RN 2679-89-2 HCA

CN Ethane-d5, 2,2'-oxybis- (9CI) (CA INDEX NAME)

RN 4472-41-7 HCA

CN Formamide-1-d, N, N-di(methyl-d3) - (7CI, 8CI, 9CI) (CA INDEX NAME)

RN 7291-22-7 HCA

CN Pyridine-d5 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$$\begin{array}{c} D \\ \end{array}$$

RN 7789-20-0 HCA

CN Water-d2 (9CI) (CA INDEX NAME)

D-- O-- D

RN 17222-37-6 HCA

CN Methane-d3, oxybis- (9CI) (CA INDEX NAME)

D3C-0-CD3

RN 7782-39-0 HCA

CN Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME)

D-- D

IC ICM C07K014-195

CC 6-3 (General Biochemistry)
Section cross-reference(s): 1, 3, 7, 9, 10

ST protein gene metab bacteria antimicrobial target; mass spectrometry protein antimicrobial target; NMR spectrometry protein antimicrobial target; x ray

crystallog protein antimicrobial target

IT Affinity chromatography
Antimicrobial agents
Bacteria (Eubacteria)
Cryoprotectants
Crystallization
Drug design

Drug targets Epitopes

Escherichia coli

Helicobacter pylori

Mass spectrometry

Molecular cloning

NMR spectroscopy

Pseudomonas aeruginosa

Staphylococcus aureus

Streptococcus pneumoniae

(bacterial polypeptides involved in carbohydrate and coenzyme metab. and their characterization as antimicrobial targets)

IT Proteins

(bacterial polypeptides involved in carbohydrate and coenzyme metab. and their characterization as antimicrobial targets)

IT Fusion proteins (chimeric proteins)

(bacterial polypeptides involved in carbohydrate and coenzyme metab. and their characterization as antimicrobial targets)

IT Gene, microbial

(coaD; bacterial **polypeptides** involved in carbohydrate and coenzyme metab. and their characterization as antimicrobial targets)

IT Hydrocarbon oils

Polyoxyalkylenes, analysis

(cryoprotectant; bacterial **polypeptides** involved in carbohydrate and coenzyme metab. and their characterization as antimicrobial targets)

IT Gene, microbial

(dfp; bacterial **polypeptides** involved in carbohydrate and coenzyme metab. and their characterization as antimicrobial targets)

IT Flavoproteins

(gene dfp; bacterial polypeptides involved in carbohydrate and coenzyme metab. and their characterization as antimicrobial targets)

IT Gene, microbial

(pgk; bacterial **polypeptides** involved in carbohydrate and coenzyme metab. and their characterization as antimicrobial targets)

IT Gene, microbial

(ribC; bacterial polypeptides involved in carbohydrate and coenzyme metab. and their characterization as antimicrobial targets)

IT Conformation

(three-dimensional structure; bacterial polypeptides involved in carbohydrate and coenzyme metab. and their characterization as antimicrobial targets)

IT Crystallography

(x-ray; bacterial polypeptides involved in carbohydrate

and coenzyme metab. and their characterization as antimicrobial targets) 110-82-7, Cyclohexane, analysis **666-52-4**, ΙT 2-Propanone-1,1,1,3,3,3-d6 811-98-3, Methanol-d4 865-49-6, Deutero-chloroform 1076-43-3, Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9 , Tetrahydrofuran-d8 2037-26-5 2206-26-0, Acetonitrile-d3 2206-27-1 2679-89-2, Diethyl ether-d10 4472-41-7, N,N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Deuterium oxide 17222-37-6 (NMR deuterium lock solvent; bacterial polypeptides involved in carbohydrate and coenzyme metab. and their characterization as antimicrobial targets) ΙT 7440-23-5, Sodium-23, analysis 7723-14-0, Phosphorus-31, analysis 7727-37-9, Nitrogen-14, analysis **7782-39-0**, Hydrogen-2, analysis 7782-41-4, Fluorine-19, analysis 10028-17-8, Hydrogen-3, analysis 12184-88-2, Hydride 14390-96-6, 14762-74-4, Carbon-13, analysis Nitrogen-15, analysis (NMR isotope label; bacterial polypeptides involved in carbohydrate and coenzyme metab. and their characterization as antimicrobial targets) 538410-08-1P 538410-10-5P 538410-12-7P, Flavoprotein (Escherichia coli gene dfp) 538410-14-9P, Flavoprotein ΙT 538410-08-1P (Escherichia coli gene dfp) 538410-16-1P 538410-17-2P 538410-19-4P (amino acid sequence; bacterial polypeptides involved in carbohydrate and coenzyme metab. and their characterization as antimicrobial targets) 9001-83-6P, Phosphoglycerate kinase 9026-37-3P, FAD synthetase ΙT 9026-99-7P, Phosphopantetheine adenylyltransferase 9032-82-0P, Riboflavin kinase (bacterial polypeptides involved in carbohydrate and coenzyme metab. and their characterization as antimicrobial targets) 56-81-5, Glycerol, analysis 64-18-6, Formic acid, analysis ΙT 77-92-9, Citric acid, analysis 67-63-0, Isopropanol, analysis 107-21-1, Ethylene glycol, analysis 107-41-5, 2-Methyl 25322-68-3, Polyethylene glycol 2,4-pentanediol (cryoprotectant; bacterial polypeptides involved in carbohydrate and coenzyme metab. and their characterization as antimicrobial targets) 7429-91-6, Dysprosium, analysis 3211-76-5, Selenomethionine ΙT 7439-88-5, Iridium, analysis 7439-90-9, Krypton, analysis 7439-91-0, Lanthanum, analysis 7439-92-1, Lead, analysis 7439-94-3, Lutetium, analysis 7439-97-6, Mercury, analysis 7439-98-7, Molybdenum, analysis 7440-00-8, Neodymium, analysis 7440-04-2, Osmium, analysis 7440-05-3, Palladium, analysis

```
7440-10-0, Praseodymium, analysis
7440-06-4, Platinum, analysis
                               7440-16-6, Rhodium, analysis
7440-15-5, Rhenium, analysis
                                7440-19-9, Samarium, analysis
7440-18-8, Ruthenium, analysis
                             7440-24-6, Strontium, analysis
7440-22-4, Silver, analysis
7440-25-7, Tantalum, analysis
                               7440-27-9, Terbium, analysis
                               7440-29-1, Thorium, analysis
7440-28-0, Thallium, analysis
7440-30-4, Thulium, analysis
                              7440-31-5, Tin, analysis
Tungsten, analysis 7440-39-3, Barium, analysis
                                                  7440-43-9,
                    7440-45-1, Cerium, analysis
                                                 7440-48-4, Cobalt,
Cadmium, analysis
          7440-52-0, Erbium, analysis
                                        7440-53-1, Europium,
analvsis
                                             7440-57-5, Gold,
           7440-54-2, Gadolinium, analysis
analysis
          7440-60-0, Holmium, analysis 7440-61-1, Uranium,
analysis
           7440-63-3, Xenon, analysis
                                       7440-64-4, Ytterbium,
analysis
          7553-56-2, Iodine, analysis 7726-95-6, Bromine,
analvsis
          7782-49-2, Selenium, analysis
analysis
   (label suitable for mass spectrometry;
   bacterial polypeptides involved in carbohydrate and
   coenzyme metab. and their characterization as antimicrobial
   targets)
59-67-6D, Nicotinic acid, protein derivs.
                                           621-82-9D, Cinnamic
acid, protein derivs.
   (matrix suitable for mass spectrometry;
   bacterial polypeptides involved in carbohydrate and
   coenzyme metab. and their characterization as antimicrobial
                                                    538410-09-2, DNA
538410-07-0, DNA (Staphylococcus aureus gene pgk)
                                  538410-11-6, DNA (Escherichia
(Staphylococcus aureus gene pgk)
                 538410-13-8, DNA (Escherichia coli gene dfp)
coli gene dfp)
538410-15-0, DNA (Staphylococcus aureus gene ribC)
                                                    538410-18-3,
DNA (Pseudomonas aeruginosa gene coaD)
                                         538410-20-7, DNA
(Pseudomonas aeruginosa gene coaD)
   (nucleotide sequence; bacterial polypeptides involved
   in carbohydrate and coenzyme metab. and their characterization as
   antimicrobial targets)
                                                        538421-69-1
              538421-49-7
                            538421-58-8
                                          538421-59-9
538421-48-6
                            538421-77-1
538421-70-4
              538421-76-0
   (unclaimed nucleotide sequence; bacterial polypeptides
   involved in carbohydrate and coenzyme metab. and their
   characterization as antimicrobial targets)
                                          538324-37-7
                                                        538324-38-8
                            538324-36-6
503534-87-0
              503534-88-1
                                          538324-42-4
                                                        538324-43-5
538324-39-9
              538324-40-2
                            538324-41-3
              538324-45-7
                          538324-46-8
                                          538324-47-9
                                                        538324-48-0
538324-44-6
   (unclaimed sequence; bacterial polypeptides involved in
   carbohydrate and coenzyme metab. and their characterization as
   antimicrobial targets)
```

L101 ANSWER 13 OF 28 HCA COPYRIGHT 2004 ACS on STN

138:283309 Cloning, purification and characterization of enzymes from

ΙT

IT

ΙT

ΙΤ

pathogenic bacteria involved in protein processing and drug screening and drug design applications. Edwards, Aled; Dharamsi, Akil; Vedadi, Masoud; Alam, Muhammad Zahoor; Awrey, Donald; Beattie, Bryan; Canadien, Veronica; Domagala, Megan; Kanagarajah, Dhushy; Li, Qin; Mansoury, Kamran; Necakov, Sasha; Nethery, Kathleen; Ng, Ivy; Pinder, Benjamin; Sheldrick, Bay; Vallee, Francois; Viola, Cristina; Wrezel, Olga (Affinium Pharmaceuticals, Inc., Can.). PCT Int. Appl. WO 2003025005 A2 20030327, 273 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). PIXXD2. APPLICATION: WO 2002-CA1426 20020920. PRIORITY: US 2001-PV324135 20010921; US 2001-PV324139 20010921; US 2001-PV325333 20010927; US 2001-PV325836 20010928; US 2001-PV338235 20011025; US 2001-PV343758 20011025; US 2001-PV340531 20011026; US 2001-PV340945 20011030; US 2001-PV333281 20011106; US 2002-PV399926 20020731. The present invention relates to polypeptide targets for pathogenic bacteria. A no. of antimicrobial target enzymes have been identified, expressed, and purified from Staphylococcus aureus, Helicobacter pylori, Streptococcus pneumoniae, and Escherichia coli. Cloning, the nucleotide sequences and the encoded amino acid sequences of genes clpL, cysM, pepP, kdsA, secA, trmD, ilvE, aroB, and glyA from S. aureus, H. pylori, S. pneumoniae, and E. coli are The invention also provides biochem. and biophys. disclosed. characteristics of those polypeptides. The polypeptides are characterized by using mass spectrometry, NMR, x-ray crystallog., and bioinformatics anal. The polypeptides of the invention can be used for drug screening, drug design, in diagnostic assays and in pharmacol. applications. 666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3, Methanol-d4 865-49-6, Chloroform-d 1076-43-3, Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9 2037-26-5 2206-26-0, Acetonitrile-d3 2206-27-1 2679-89-2 4472-41-7, N, N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Water-d2 17222-37-6 (deuterium lock solvent; cloning, purifn. and characterization of enzymes from pathogenic bacteria involved in protein processing, and drug screening and drug design applications)

AB

ΙT

RN

666-52-4

HCA

CN 2-Propanone-1,1,1,3,3,3-d6 (9CI) (CA INDEX NAME)

D3C-C-CD3

RN 811-98-3 HCA

CN Methanol-d4 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

D3C-0-D

RN 865-49-6 HCA

CN Methane-d, trichloro- (9CI) (CA INDEX NAME)

C1-C-C1

RN 1076-43-3 HCA

CN Benzene-d6 (8CI, 9CI) (CA INDEX NAME)

 $\begin{array}{c} D \\ D \\ D \end{array}$

RN 1516-08-1 HCA

CN Ethanol-d6 (9CI) (CA INDEX NAME)

D3C-CD2-O-D

RN 1665-00-5 HCA

CN Methane-d2, dichloro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 1693-74-9 HCA

CN Furan-d4, tetrahydro-d4- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$$D \qquad D \qquad D$$

RN 2037-26-5 HCA

CN Benzene-d5, methyl-d3- (9CI) (CA INDEX NAME)

RN 2206-26-0 HCA

CN Acetonitrile-d3 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 2206-27-1 HCA

CN Methane-d3, sulfinylbis- (9CI) (CA INDEX NAME)

RN 2679-89-2 HCA

CN Ethane-d5, 2,2'-oxybis- (9CI) (CA INDEX NAME)

D3C-CD2-O-CD2-CD3

RN 4472-41-7 HCA

CN Formamide-1-d, N,N-di(methyl-d3)- (7CI, 8CI, 9CI) (CA INDEX NAME)

RN 7291-22-7 HCA

CN Pyridine-d5 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$$\begin{array}{c} D \\ \end{array}$$

RN 7789-20-0 HCA

CN Water-d2 (9CI) (CA INDEX NAME)

D- O- D

RN 17222-37-6 HCA

CN Methane-d3, oxybis- (9CI) (CA INDEX NAME)

D3C- O- CD3

IT 7782-39-0, Hydrogen-2, uses

(isotope label; cloning, purifn. and characterization of enzymes from pathogenic bacteria involved in protein processing, and drug screening and drug design applications)

RN 7782-39-0 HCA

Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME) CN D— D ICM C07K014-195 IC CC 7-2 (Enzymes) Section cross-reference(s): 1, 3, 10, 63 ΙT Antibacterial agents Bioinformatics Cryoprotectants Crystal growth Crystal morphology DNA sequences Drug design Drug screening Escherichia coli Exchange reaction Gel electrophoresis Helicobacter pylori Mass spectrometry Molecular cloning NMR (nuclear magnetic resonance) NMR spectroscopy Pathogenic bacteria Post-translational processing Protein sequences Solubility Stability Staphylococcus aureus Streptococcus pneumoniae X-ray diffractometry (cloning, purifn. and characterization of enzymes from pathogenic bacteria involved in protein processing, and drug screening and drug design applications) Molecular association TΤ (identification of interacting proteins; cloning, purifn. and characterization of enzymes from pathogenic bacteria involved in protein processing, and drug screening and drug design applications) ΙT Polyoxyalkylenes, uses (low-mol.-wt., cryoprotectant; cloning, purifn. and characterization of enzymes from pathogenic bacteria involved in protein processing, and drug screening and drug design applications) ΙT 110-82-7, Cyclohexane, uses 666-52-4, 2-Propanone-1,1,1,3,3,3-d6 **811-98-3**, Methanol-d4 **865-49-6**,

Chloroform-d 1076-43-3, Benzene-d6 1516-08-1,

Ethanol-d6 1665-00-5 1693-74-9 2037-26-5 2206-26-0, Acetonitrile-d3 2206-27-1 2679-89-2 4472-41-7, N,N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Water-d2 17222-37-6

(deuterium lock solvent; cloning, purifn. and characterization of enzymes from pathogenic bacteria involved in protein processing, and drug screening and drug design applications)

IT 1333-74-0, Hydrogen, uses 7440-23-5, Sodium-23, uses 7723-14-0, Phosphorus-31, uses 7727-37-9, Nitrogen-14, uses **7782-39-0**, Hydrogen-2, uses 7782-41-4, Fluorine-19, uses 10028-17-8, Hydrogen-3, uses 14390-96-6, Nitrogen-15, uses 14762-74-4, Carbon-13, uses

(isotope label; cloning, purifn. and characterization of enzymes from pathogenic bacteria involved in protein processing, and drug screening and drug design applications)

IT 25322-68-3, **PEG**

(low-mol.-wt., cryoprotectant; cloning, purifn. and characterization of enzymes from pathogenic bacteria involved in protein processing, and drug screening and drug design applications)

IT 59-67-6D, Nicotinic acid, derivs.

(mass spectrometric matrix; cloning, purifn. and characterization of enzymes from pathogenic bacteria involved in protein processing, and drug screening and drug design applications)

L101 ANSWER 14 OF 28 HCA COPYRIGHT 2004 ACS on STN 138:283070 Purification of enzymes involved in protein synthesis from pathogenic bacteria for characterization in development of targets for antibiotics. Edwards, Aled; Dharamsi, Akil; Vedadi, Masoud; Alam, Muhammad Zahoor; Awrey, Donald; Beattie, Bryan; Canadien, Veronica; Domagala, Megan; Houston, Simon; Kanagarajah, Dhushy; Necakov, Sasha; Nethery, Kathleen; Ng, Ivy; Mansoury, Kamran; McDonald, Merry-Lynn; Pinder, Benjamin; Sheldrick, Bay; Viola, Cristina (Affinium Pharmaceuticals, Inc., Can.). PCT Int. Appl. WO 2003025008 A2 20030327, 254 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-CA1429 20020920. PRIORITY: US 2001-PV324176 20010921; US 2001-PV324439 20010924; US 2001-PV324713 20010925; US

2001-PV324690 20010925; US 2001-PV326336 20011001; US 2001-PV341466 20011217; US 2001-PV341764 20011218; US 2001-PV341918 20011219. Methods of purifying and characterizing enzymes that may play a role AB in protein synthesis in pathogenic bacteria are described. The proteins may be useful as targets for antibiotics and methods for identifying regions of the proteins that may be targeted by drugs are described. The invention also provides biochem. and biophys. characteristics of those polypeptides. 666-52-4, Perdeuteroacetone 811-98-3, Methanol-d4 ΙT 865-49-6, Deuterochloroform 1076-43-3, Perdeuterobenzene 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9, Perdeuterotetrahydrofuran 2037-26-5 2206-26-0, Perdeuteroacetonitrile 2206-27-1, Dimethylsulfoxide-d6 2679-89-2, Diethyl ether-d10 4472-41-7, N,N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Heavy water 17222-37-6 (as deuterium lock solvent in NMR of proteins; purifn. of enzymes involved in protein synthesis from pathogenic bacteria for characterization in development of targets for antibiotics) RN 2-Propanone-1,1,1,3,3,3-d6 (9CI) (CA INDEX NAME) CN D3C-C-CD3 811-98-3 HCA RN Methanol-d4 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME) CN D3C-O-D 865-49-6 HCA RNMethane-d, trichloro- (9CI) (CA INDEX NAME) CNCl

1076-43-3 HCA

Benzene-d6 (8CI, 9CI) (CA INDEX NAME)

RN

CN

$$D \qquad D \qquad D$$

RN 1516-08-1 HCA

CN Ethanol-d6 (9CI) (CA INDEX NAME)

D3C-CD2-O-D

RN 1665-00-5 HCA

CN Methane-d2, dichloro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 1693-74-9 HCA

CN Furan-d4, tetrahydro-d4- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 2037-26-5 HCA

CN Benzene-d5, methyl-d3- (9CI) (CA INDEX NAME)

RN 2206-26-0 HCA CN Acetonitrile-d3 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 2206-27-1 HCA

CN Methane-d3, sulfinylbis- (9CI) (CA INDEX NAME)

RN 2679-89-2 HCA

CN Ethane-d5, 2,2'-oxybis- (9CI) (CA INDEX NAME)

D3C-CD2-O-CD2-CD3

RN 4472-41-7 HCA

CN Formamide-1-d, N, N-di(methyl-d3)- (7CI, 8CI, 9CI) (CA INDEX NAME)

RN 7291-22-7 HCA

CN Pyridine-d5 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

```
\begin{array}{c} D \\ \end{array}
```

RN 7789-20-0 HCA

CN Water-d2 (9CI) (CA INDEX NAME)

D- O- D

RN 17222-37-6 HCA

CN Methane-d3, oxybis- (9CI) (CA INDEX NAME)

D3C-0-CD3

7782-39-0, Deuterium, biological studies
(as isotopic label for NMR of proteins; purifn. of
enzymes involved in protein synthesis from pathogenic bacteria
for characterization in development of targets for antibiotics)

RN 7782-39-0 HCA

CN Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME)

D-- D

IC ICM C07K014-195

CC 6-3 (General Biochemistry)
Section cross-reference(s): 1, 3, 10

ST enzyme purifn NMR mass spectrometry genomics protein synthesis; protein processing enzyme antibiotic design selection

IT Hydrocarbon oils

Polyoxyalkylenes, biological studies
(as cryoprotectant; purifn. of enzymes involved in protein synthesis from pathogenic bacteria for characterization in development of targets for antibiotics)

IT NMR spectroscopy

(deuterium; purifn. of enzymes involved in protein synthesis from pathogenic bacteria for characterization in development of targets for antibiotics)

IT Crystallization

Mass spectrometry

(of proteins; purifn. of enzymes involved in protein synthesis from pathogenic bacteria for characterization in development of targets for antibiotics) 56-81-5, Glycerol, biological studies 64-18-6, Formic acid, ΙT 67-63-0, Isopropanol, biological studies biological studies 77-92-9, Citric acid, biological studies 107-21-1, Ethylene glycol, biological studies 5683-44-3, 3-Methyl-2,4-pentanediol 25322-68-3, Polyethylene glycol (as cryoprotectant; purifn. of enzymes involved in protein synthesis from pathogenic bacteria for characterization in development of targets for antibiotics) 110-82-7, Cyclohexane, analysis 666-52-4, ITPerdeuteroacetone 811-98-3, Methanol-d4 865-49-6 , Deuterochloroform 1076-43-3, Perdeuterobenzene 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9 , Perdeuterotetrahydrofuran 2037-26-5 2206-26-0, Perdeuteroacetonitrile 2206-27-1, Dimethylsulfoxide-d6 2679-89-2, Diethyl ether-d10 4472-41-7, N, N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Heavy water 17222-37-6 (as deuterium lock solvent in NMR of proteins; purifn. of enzymes involved in protein synthesis from pathogenic bacteria for characterization in development of targets for antibiotics) ΙT 1333-74-0, Hydrogen, biological studies 7440-23-5, Sodium-23,

1333-74-0, Hydrogen, biological studies 7440-23-5, Sodium-23, biological studies 7723-14-0, Phosphorus-31, biological studies 7727-37-9, Nitrogen 14, biological studies 7782-39-0, Deuterium, biological studies 7782-41-4, Fluorine-19, biological studies 10028-17-8, Tritium, biological studies 14390-96-6, Nitrogen 15, biological studies 14762-74-4, Carbon 13, biological studies

(as **isotopic** label for NMR of proteins; purifn. of enzymes involved in protein synthesis from pathogenic bacteria for characterization in development of targets for antibiotics)

L101 ANSWER 15 OF 28 HCA COPYRIGHT 2004 ACS on STN

138:283069 Purification of proteins of microbial cell wall biosynthesis from pathogenic bacteria for characterization in development of targets for antibiotics. Edwards, Aled; Dharamsi, Akil; Vedadi, Masoud; Alam, Muhammad Zahoor; Awrey, Donald; Beattie, Bryan; Domagala, Megan; Houston, Simon; Kanagarajah, Dhushy; Nethery, Kathleen; Ng, Ivy; Mansoury, Kamran; McDonald, Merry-Lynn; Pinder, Benjamin; Viola, Cristina; Wrezel, Olga (Affinium Pharmaceuticals, Inc., Can.). PCT Int. Appl. WO 2003025007 A2 20030327, 325 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT,

TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-CA1428 20020920. PRIORITY: US 2001-PV324152 20010921; US 2001-PV323992 20010921; US 2001-PV324692 20010925; US 2001-PV3339924 20011026; US 2001-PV350973 20011029; US 2001-PV340924 20011030; US 2001-PV333666 20011127; US 2001-PV341732 20011218; US 2001-PV341776 20011218; US 2001-PV341949 20011219.

AB Methods of purifying and characterizing enzymes that may play a role in microbial cell wall biosynthesis in pathogenic bacteria are described. The proteins may be useful as targets for antibiotics and methods for identifying regions of the proteins that may be targeted by drugs are described. The invention also provides biochem. and biophys. characteristics of those polypeptides

IT 666-52-4, Perdeuteroacetone 811-98-3, Methanol-d4
865-49-6, Deuterochloroform 1076-43-3,
Perdeuterobenzene 1516-08-1, Ethanol-d6 1665-00-5
1693-74-9, Perdeuterotetrahydrofuran 2037-26-5
2206-26-0, Perdeuteroacetonitrile 2206-27-1,
Dimethylsulfoxide-d6 2679-89-2, Diethyl ether-d10
4472-41-7, N,N-Dimethylformamide-d7 7291-22-7,
Pyridine-d5 7789-20-0, Heavy water 17222-37-6
(as deuterium lock solvent in NMR of proteins; purifn.
of proteins of microbial cell wall biosynthesis from pathogenic bacteria for characterization in development of targets for antibiotics)

RN 666-52-4 HCA

CN 2-Propanone-1,1,1,3,3,3-d6 (9CI) (CA INDEX NAME)

RN 811-98-3 HCA CN Methanol-d4 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

D3C-0-D

RN 865-49-6 HCA

CN Methane-d, trichloro- (9CI) (CA INDEX NAME)

RN 1076-43-3 HCA

CN Benzene-d6 (8CI, 9CI) (CA INDEX NAME)

$$\begin{array}{c} D \\ D \\ D \\ \end{array}$$

RN 1516-08-1 HCA

CN Ethanol-d6 (9CI) (CA INDEX NAME)

D3C-CD2-O-D

RN 1665-00-5 HCA

CN Methane-d2, dichloro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 1693-74-9 HCA

CN Furan-d4, tetrahydro-d4- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 2037-26-5 HCA

CN Benzene-d5, methyl-d3- (9CI) (CA INDEX NAME)

RN 2206-26-0 HCA

CN Acetonitrile-d3 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 2206-27-1 HCA

CN Methane-d3, sulfinylbis- (9CI) (CA INDEX NAME)

RN 2679-89-2 HCA

CN Ethane-d5, 2,2'-oxybis- (9CI) (CA INDEX NAME)

D3C-CD2-O-CD2-CD3

RN 4472-41-7 HCA

CN Formamide-1-d, N, N-di(methyl-d3) - (7CI, 8CI, 9CI) (CA INDEX NAME)

RN 7291-22-7 HCA

CN Pyridine-d5 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$$\begin{array}{c} D \\ \end{array}$$

RN 7789-20-0 HCA

CN Water-d2 (9CI) (CA INDEX NAME)

D- O- D

RN 17222-37-6 HCA

CN Methane-d3, oxybis- (9CI) (CA INDEX NAME)

D3C-0-CD3

7782-39-0, Deuterium, biological studies
 (as isotopic label for NMR of proteins; purifn. of
 proteins of microbial cell wall biosynthesis from pathogenic
 bacteria for characterization in development of targets for
 antibiotics)

RN 7782-39-0 HCA

CN Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME)

D-D

IC ICM C07K014-195

CC 6-3 (General Biochemistry)
Section cross-reference(s): 1, 3, 10

ST enzyme purifn NMR mass spectrometry genomics; microbial cell wall biosynthesis enzyme antibiotic design selection

IT Hydrocarbon oils

Polyoxyalkylenes, biological studies

(as cryoprotectant; purifn. of proteins of microbial cell wall biosynthesis from pathogenic bacteria for characterization in development of targets for antibiotics)

IT NMR spectroscopy

(deuterium; purifn. of proteins of microbial cell wall biosynthesis from pathogenic bacteria for characterization in development of targets for antibiotics)

IT Crystallization

Mass spectrometry

(of proteins; purifn. of proteins of microbial cell

wall biosynthesis from pathogenic bacteria for characterization in development of targets for antibiotics)

IT 56-81-5, Glycerol, biological studies 64-18-6, Formic acid, biological studies 67-63-0, Isopropanol, biological studies 77-92-9, Citric acid, biological studies 107-21-1, Ethylene glycol, biological studies 5683-44-3, 3-Methyl-2,4-pentanediol 25322-68-3, Polyethylene glycol

(as cryoprotectant; purifn. of proteins of microbial cell wall biosynthesis from pathogenic bacteria for characterization in development of targets for antibiotics)

IT 110-82-7, Cyclohexane, analysis 666-52-4, Perdeuteroacetone 811-98-3, Methanol-d4 865-49-6, Deuterochloroform 1076-43-3, Perdeuterobenzene 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9, Perdeuterotetrahydrofuran 2037-26-5 2206-26-0, Perdeuteroacetonitrile 2206-27-1, Dimethylsulfoxide-d6 2679-89-2, Diethyl ether-d10 4472-41-7, N,N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Heavy water 17222-37-6

(as deuterium lock solvent in NMR of proteins; purifn. of proteins of microbial cell wall biosynthesis from pathogenic bacteria for characterization in development of targets for antibiotics)

IT 1333-74-0, Hydrogen, biological studies 7440-23-5, Sodium-23, biological studies 7723-14-0, Phosphorus-31, biological studies 7727-37-9, Nitrogen 14, biological studies 7782-39-0, Deuterium, biological studies 7782-41-4, Fluorine-19, biological studies 10028-17-8, Tritium, biological studies 14390-96-6, Nitrogen 15, biological studies 14762-74-4, Carbon 13, biological studies

(as **isotopic** label for NMR of proteins; purifn. of proteins of microbial cell wall biosynthesis from pathogenic bacteria for characterization in development of targets for antibiotics)

L101 ANSWER 16 OF 28 HCA COPYRIGHT 2004 ACS on STN

138:282444 Cloning, purification and characterization of

polypeptides from pathogenic bacteria involved in membrane
biosynthesis, and drug screening and drug design applications.
Edwards, Aled; Dharamsi, Akil; Vedadi, Masoud; Alam, Muhammad
Zahoor; Awrey, Donald; Beattie, Bryan; Canadien, Veronica; Domagala,
Megan; Houston, Simon; Kanagarajah, Dhushy; Li, Qin; Mansoury,
Kamran; McDonald, Merry-Lynn; Necakov, Sasha; Ng, Ivy; Pinder,
Benjamin; Sheldrick, Bay; Vallee, Francois; Viola, Cristina; Wrezel,
Olga (Affinium Pharmaceuticals, Inc., Can.). PCT Int. Appl. WO
2003027139 A2 20030403, 312 pp. DESIGNATED STATES: W: AE, AG, AL,
AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ,
DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,

```
IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-CA1443 20020924. PRIORITY: US 2001-PV324449 20010924; US 2001-PV324504 20010924; US 2001-PV326269 20011001; US 2001-PV326887 20011003; US 2001-PV339560 20011024; US 2001-PV337471 20011025; US 2001-PV340002 20011026; US 2001-PV340000 20011026; US 2001-PV340027 20011026; US 2001-PV341767 20011218; US 2001-PV344307 20011221; US 2001-PV343946 20011227. The present invention relates to polypeptide targets for pathogenic bacteria. A no. of antimicrobial target enzymes and
```

The present invention relates to polypeptide targets for pathogenic bacteria. A no. of antimicrobial target enzymes and proteins have been identified, expressed, and purified from Staphylococcus aureus, Helicobacter pylori, Streptococcus pneumoniae, and Pseudomonas aeruginosa. Cloning, the nucleotide sequences and the encoded amino acid sequences of genes ftsZ, fabZ, acpS, murD, murC, fabH, tagD, obg, and fabG from S. aureus, H. pylori, S. pneumoniae, and P. aeruginosa are disclosed. The invention also provides biochem. and biophys. characteristics of those polypeptides. The polypeptides are characterized by using mass spectrometry, NMR, x-ray crystallog., and bioinformatics anal. The polypeptides of the invention can be used for drug screening, drug design, in diagnostic assays and in pharmacol. applications.

IT 666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3, Methanol-d4 865-49-6, Chloroform-d 1076-43-3, Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9 2037-26-5 2206-26-0, Acetonitrile-d3 2206-27-1 2679-89-2 4472-41-7, N,N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Water-d2 17222-37-6

(deuterium lock solvent; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

RN 666-52-4 HCA

2-Propanone-1,1,1,3,3,3-d6 (9CI) (CA INDEX NAME)

CN

RN 811-98-3 HCA

CN Methanol-d4 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

D3C - O - D

RN 865-49-6 HCA

CN Methane-d, trichloro- (9CI) (CA INDEX NAME)

RN 1076-43-3 HCA

CN Benzene-d6 (8CI, 9CI) (CA INDEX NAME)

$$\begin{array}{c} D \\ D \\ D \\ \end{array}$$

RN 1516-08-1 HCA

CN Ethanol-d6 (9CI) (CA INDEX NAME)

D3C-CD2-O-D

RN 1665-00-5 HCA

CN Methane-d2, dichloro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 1693-74-9 HCA

CN Furan-d4, tetrahydro-d4- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$$D \qquad D \qquad D$$

RN 2037-26-5 HCA

CN Benzene-d5, methyl-d3- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} D & CD3 \\ \hline \end{array}$$

RN 2206-26-0 HCA

CN Acetonitrile-d3 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 2206-27-1 HCA

CN Methane-d3, sulfinylbis- (9CI) (CA INDEX NAME)

RN 2679-89-2 HCA

CN Ethane-d5, 2,2'-oxybis- (9CI) (CA INDEX NAME)

D3C-CD2-O-CD2-CD3

RN 4472-41-7 HCA

CN Formamide-1-d, N, N-di(methyl-d3) - (7CI, 8CI, 9CI) (CA INDEX NAME)

```
D3C-N-C-D
RN
     7291-22-7 HCA
     Pyridine-d5 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)
CN
RN
     7789-20-0 HCA
CN
     Water-d2 (9CI) (CA INDEX NAME)
D- O- D
     17222-37-6 HCA
RN
    Methane-d3, oxybis- (9CI) (CA INDEX NAME)
CN
D3C-0-CD3
ΙT
     7782-39-0, Hydrogen-2, uses
        (isotope label; cloning, purifn. and characterization
        of polypeptides from pathogenic bacteria involved in
        membrane biosynthesis, and drug screening and drug design
        applications)
     7782-39-0 HCA
RN
CN
     Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME)
D-D
     ICM C07K014-195
IC
     3-3 (Biochemical Genetics)
CC
     Section cross-reference(s): 1, 6, 7, 10, 63
ΙΤ
     Proteins
        (16,000-mol.-wt., compn. contg. 3-Oxoacyl-[acyl carrier protein]
        synthase III and; cloning, purifn. and characterization of
        polypeptides from pathogenic bacteria involved in
```

membrane biosynthesis, and drug screening and drug design

applications)

- IT Proteins
 - (25,000-mol.-wt., compn. contg. 3-oxoacyl-[acyl carrier protein] reductase and; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)
- IT Proteins

(FTSA, compn. contg. FtsZ protein and; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

- IT Ribosomal proteins
 - (L1, compn. contg. FtsZ protein and; cloning, purifn. and characterization of **polypeptides** from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)
- IT Ribosomal proteins
 - (L16, compn. contg. gene obg protein and; cloning, purifn. and characterization of **polypeptides** from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)
- IT Ribosomal proteins
 - (L2, compn. contg. FtsZ protein and; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)
- IT Ribosomal proteins
 - (L22, compn. contg. FtsZ protein and; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)
- IT Ribosomal proteins
 - (L3, compn. contg. FtsZ protein and; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)
- IT Ribosomal proteins
 - (L4, compn. contg. FtsZ protein and; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)
- IT Ribosomal proteins
 - (L5, compn. contg. FtsZ protein and; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)
- IT Ribosomal proteins

(L6, compn. contg. FtsZ protein and; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

IT Ribosomal proteins

(S2, compn. contg. FtsZ protein and; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

IT Ribosomal proteins

(S4, compn. contg. FtsZ protein and; cloning, purifn. and characterization of **polypeptides** from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

IT Ribosomal proteins

(S5, compn. contg. FtsZ protein and; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

IT Ribosomal proteins

(S7, compn. contg. FtsZ protein and; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

IT Gene, microbial

(acpS; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

IT Infection

(bacterial; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

IT Membrane, biological

(bilayer; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

IT Antibacterial agents
Bioinformatics
Cryoprotectants
Crystal growth
Crystal morphology
DNA sequences
Drug design
Drug screening
Exchange reaction

Gel electrophoresis Helicobacter pylori Mass spectrometry Molecular cloning NMR (nuclear magnetic resonance) NMR spectroscopy Pathogenic bacteria Protein sequences Pseudomonas aeruginosa Solubility Stability Staphylococcus aureus Streptococcus pneumoniae X-ray diffractometry (cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications) Fusion proteins (chimeric proteins) (cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications) Paraffin oils (cryoprotectant; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications) Gene, microbial (fabG; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications) Gene, microbial (fabH; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications) Gene, microbial (fabZ; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications) Proteins (ftsZ, Staphylococcus aureus; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

ΙT

ΙΤ

ΙΤ

ΙT

ΙT

ΙT

ΙT

Gene, microbial

(ftsZ; cloning, purifn. and characterization of

polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

IT Proteins

(gene obg, Staphylococcus aureus; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

IT Proteins

(gene tagD, Staphylococcus aureus; cloning, purifn. and characterization of **polypeptides** from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

IT Elements

(heavy, label; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

IT Molecular association

(identification of interacting proteins; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

IT Toxins

(leukotoxins, LukM, compn. contg.; cloning, purifn. and characterization of **polypeptides** from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

IT Polyoxyalkylenes, uses

(low-mol.-wt., cryoprotectant; cloning, purifn. and characterization of **polypeptides** from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

IT Epitopes

(mapping; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

IT Gene, microbial

(murC; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

IT Gene, microbial

(murD; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

- Organic compounds, biological studies

 (polypeptides complexed with; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)
- IT Gene, microbial (tagD; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)
- IT Genome
 (virtual genome anal.; cloning, purifn. and characterization of
 polypeptides from pathogenic bacteria involved in
 membrane biosynthesis, and drug screening and drug design
 applications)
- 9030-86-8P, (3R)-Hydroxymyristoyl-[acyl-carrier protein] dehydratase ((3R)-Hydroxymyristoyl-[acyl-carrier protein] dehydratase, of Staphylococcus aureus; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)
- 9023-52-3P, Gene murC enzyme 9023-59-0P, UDP-N-acetylmuramoylalanine-D-glutamate ligase
 (H. pylori; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)
- 37250-34-3P, 3-Ketoacyl acyl carrier protein reductase (Helicobacter pylori and Pseudomonas aeruginosa; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)
- 9077-10-5P, 3-Oxoacyl-[acyl carrier protein] synthase
 (III, Staphylococcus aureus; cloning, purifn. and
 characterization of polypeptides from pathogenic
 bacteria involved in membrane biosynthesis, and drug screening
 and drug design applications)
- IT 37278-30-1P, Acyl carrier protein synthase

```
(Staphylococcus aureus and Streptococcus pneumoniae; cloning,
       purifn. and characterization of polypeptides from
       pathogenic bacteria involved in membrane biosynthesis, and drug
        screening and drug design applications)
     503876-73-1DP, subfragments and variants are claimed
ΙT
     503876-74-2DP, subfragments and variants are claimed
     503876-75-3DP, subfragments and variants are claimed
     503876-76-4DP, subfragments and variants are claimed
     503876-77-5DP, subfragments and variants are claimed
     503876-78-6DP, subfragments and variants are claimed
     503876-79-7DP, subfragments and variants are claimed
     503882-88-0DP, subfragments and variants are claimed
     504444-78-4DP, Protein (Staphylococcus aureus gene obg),
    subfragments and variants are claimed
                                             504444-79-5DP, subfragments
                               504444-80-8DP, subfragments and variants
    and variants are claimed
                   504444-81-9DP, subfragments and variants are claimed
    are claimed
        (amino acid sequence; cloning, purifn. and characterization of
       polypeptides from pathogenic bacteria involved in
       membrane biosynthesis, and drug screening and drug design
        applications)
ΙT
    9014-24-8, RNA polymerase
        (compn. contg. FtsZ protein and; cloning, purifn. and
       characterization of polypeptides from pathogenic
       bacteria involved in membrane biosynthesis, and drug screening
        and drug design applications)
ΙT
     56-81-5, Glycerol, uses 64-18-6, Formic acid, uses 67-63-0,
                         77-92-9, Citric acid, uses 107-21-1, Ethylene
     Isopropanol, uses
     glycol, uses
                    107-41-5
        (cryoprotectant; cloning, purifn. and characterization of
       polypeptides from pathogenic bacteria involved in
       membrane biosynthesis, and drug screening and drug design
        applications)
     110-82-7, Cyclohexane, uses 666-52-4, 2-Propanone-
ΙT
     1,1,1,3,3,3-d6 811-98-3, Methanol-d4 865-49-6,
     Chloroform-d 1076-43-3, Benzene-d6 1516-08-1,
     Ethanol-d6 1665-00-5 1693-74-9 2037-26-5
     2206-26-0, Acetonitrile-d3 2206-27-1
     2679-89-2 4472-41-7, N, N-Dimethylformamide-d7
     7291-22-7, Pyridine-d5 7789-20-0, Water-d2
     17222-37-6
        (deuterium lock solvent; cloning, purifn. and
        characterization of polypeptides from pathogenic
        bacteria involved in membrane biosynthesis, and drug screening
        and drug design applications)
     7429-91-6, Dysprosium, uses 7439-88-5, Iridium, uses
                                                              7439-90-9,
ΙΤ
     Krypton, uses 7439-91-0, Lanthanum, uses 7439-92-1, Lead, uses
     7439-94-3, Lutetium, uses 7439-97-6, Mercury, uses 7439-98-7,
```

Molybdenum, uses 7440-00-8, Neodymium, uses 7440-04-2, Osmium,

7440-05-3, Palladium, uses 7440-06-4, Platinum, uses uses 7440-10-0, Praseodymium, uses 7440-15-5, Rhenium, uses 7440-16-6, Rhodium, uses 7440-18-8, Ruthenium, uses 7440-19-9, Samarium, uses 7440-22-4, Silver, uses 7440-24-6, Strontium, 7440-25-7, Tantalum, uses 7440-27-9, Terbium, uses 7440-28-0, Thallium, uses 7440-29-1, Thorium, uses 7440-30-4, 7440-31-5, Tin, uses 7440-33-7, Tungsten, uses Thulium, uses 7440-39-3, Barium, uses 7440-43-9, Cadmium, uses 7440-45-1, 7440-48-4, Cobalt, uses 7440-52-0, Erbium, uses Cerium, uses 7440-53-1, Europium, uses 7440-54-2, Gadolinium, uses 7440-57-5, 7440-60-0, Holmium, uses 7440-61-1, Uranium, uses Gold, uses 7440-63-3, Xenon, uses 7440-64-4, Ytterbium, uses 7553-56-2, Iodine, uses 7726-95-6, Bromine, uses 7782-49-2, Selenium, uses (heavy atom label; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

1333-74-0, Hydrogen, uses 7440-23-5, Sodium-23, uses 7723-14-0, Phosphorus-31, uses 7727-37-9, Nitrogen-14, uses **7782-39-0**, Hydrogen-2, uses 7782-41-4, Fluorine-19, uses 10028-17-8, Hydrogen-3, uses 14390-96-6, Nitrogen-15, uses 14762-74-4, Carbon-13, uses

(isotope label; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

ΙΤ

25322-68-3, PEG
(low-mol.-wt., cryoprotectant; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

IT 59-67-6D, Nicotinic acid, derivs. 621-82-9D, Cinnamic acid, derivs.

(mass spectrometric matrix; cloning, purifn. and characterization of polypeptides from pathogenic bacteria involved in membrane biosynthesis, and drug screening and drug design applications)

503876-65-1D, DNA (Staphylococcus aureus gene ftsZ), subfragments and variants are claimed 503876-66-2D, DNA (Staphylococcus aureus gene fabZ), subfragments and variants are claimed 503876-67-3D, DNA (Helicobacter pylori gene fabG), subfragments and variants are claimed 503876-68-4D, DNA (Staphylococcus aureus gene acpS), subfragments and variants are claimed 503876-69-5D, DNA

```
(Helicobacter pylori gene murD), subfragments and variants are
          503876-70-8D, DNA (Helicobacter pylori gene murC),
subfragments and variants are claimed
                                        503876-71-9D, DNA
(Staphylococcus aureus gene fabH), subfragments and variants are
          503876-72-0D, DNA (Staphylococcus aureus gene taqD),
subfragments and variants are claimed
                                        504444-74-0D, DNA
(Staphylococcus aureus gene obg), subfragments and variants are
          504444-75-1D, subfragments and variants are claimed
504444-76-2D, subfragments and variants are claimed
                                                    504444-77-3D,
subfragments and variants are claimed
   (nucleotide sequence; cloning, purifn. and characterization of
  polypeptides from pathogenic bacteria involved in
  membrane biosynthesis, and drug screening and drug design
  applications)
504489-14-9
              504489-16-1
                            504489-17-2
                                          504489-19-4
                                                        504489-21-8
                                                        504489-30-9
                            504489-25-2
                                          504489-29-6
              504489-24-1
504489-23-0
   (unclaimed nucleotide sequence; cloning, purifn. and
   characterization of polypeptides from pathogenic
  bacteria involved in membrane biosynthesis, and drug screening
   and drug design applications)
                            504489-22-9
              504489-18-3
504489-15-0
   (unclaimed protein sequence; cloning, purifn. and
   characterization of polypeptides from pathogenic
  bacteria involved in membrane biosynthesis, and drug screening
   and drug design applications)
                                          503882-59-5
                                                        503882-60-8
              503882-57-3
                            503882-58-4
503534-88-1
                                                        503882-65-3
                                          503882-64-2
503882-61-9
              503882-62-0
                            503882-63-1
                                          503882-69-7
                                                        503882-70-0
                            503882-68-6
503882-66-4
              503882-67-5
              503882-72-2
                            503882-73-3
                                          503882-74-4
                                                        503882-75-5
503882-71-1
                                                        503882-80-2
              503882-77-7
                            503882-78-8
                                          503882-79-9
503882-76-6
                                                        503882-85-7
                            503882-83-5
                                          503882-84-6
503882-81-3
              503882-82-4
503882-86-8 503882-87-9
                                          503882-90-4
                                                        504406-77-3
                            503882-89-1
                                                        504406-82-0
              504406-79-5
                            504406-80-8
                                          504406-81-9
504406-78-4
                                          504406-86-4
                                                        504406-87-5
                            504406-85-3
504406-83-1
              504406-84-2
                            504406-90-0
                                          504406-91-1
                                                        504406-92-2
504406-88-6
              504406-89-7
                                                        504406-97-7
504406-93-3
              504406-94-4
                            504406-95-5
                                          504406-96-6
                                          504410-38-2
                                                        504410-39-3
                            504410-37-1
504410-35-9
              504410-36-0
              504410-41-7
                            504410-42-8
                                          504410-43-9
                                                        504410-44-0
504410-40-6
                                          504410-48-4
                                                        504410-49-5
              504410-46-2
                            504410-47-3
504410-45-1
```

(unclaimed sequence; cloning, purifn. and characterization of

membrane biosynthesis, and drug screening and drug design

IT

ΙT

ΙΤ

504489-20-7

applications)

L101 ANSWER 17 OF 28 HCA COPYRIGHT 2004 ACS on STN 138:282426 Cloning, purification and characterization of polypeptides from pathogenic bacteria involved in nucleic

polypeptides from pathogenic bacteria involved in

acid processing and drug screening and drug design applications. Edwards, Aled; Dharamsi, Akil; Vedadi, Masoud; Alam, Muhammad Zahoor; Arrowsmith, Cheryl; Awrey, Donald; Beattie, Bryan; Canadien, Veronica; Cox, Brian; Domagala, Megan; Houston, Simon; Li, Qin; Nethery, Kathleen; Ng, Ivy; Ouyang, Hui; Pinder, Benjamin; Sheldrick, Bay; Viola, Cristina; Wrezel, Olga (Affinium Pharmaceuticals, Inc., Can.). PCT Int. Appl. WO 2003025004 A2 20030327, 298 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-CA1411 20020918. PRIORITY: US 2001-PV323040 20010918; US 2001-PV325307 20010927; US 2001-PV325421 20010927; US 2001-PV325891 20010928; US 2001-PV326337 20011001; US 2001-PV326774 20011003; US 2001-PV327193 20011004; US 2001-PV340922 20011030; US 2001-PV338709 20011105; US 2001-PV333269 20011106; US 2001-PV341679 20011218.

The present invention relates to polypeptide targets for AB pathogenic bacteria. A no. of antimicrobial target enzymes and proteins have been identified, expressed, and purified from Staphylococcus aureus, Helicobacter pylori, Streptococcus pneumoniae, and Pseudomonas aeruginosa. Cloning, the nucleotide sequences and the encoded amino acid sequences of genes nrdE, pyrH, pnpA, ung, rho, pnp, pyrE, lig, dnaN, nrdF, and nrdE from S. aureus, H. pylori, S. pneumoniae, and P. aeruginosa are disclosed. The invention also provides biochem. and biophys. characteristics of those polypeptides. The polypeptides are characterized by using mass spectrometry, NMR, x-ray crystallog., and bioinformatics The polypeptides of the invention can be used for drug screening, drug design, in diagnostic assays and in pharmacol. applications.

IT 666-52-4, 2-Propanone-1,1,1,3,3,3-d6 811-98-3, Methanol-d4 865-49-6, Chloroform-d 1076-43-3, Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9 2037-26-5 2206-26-0, Acetonitrile-d3 2206-27-1 2679-89-2 4472-41-7, N,N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Heavy water 17222-37-6

(deuterium lock solvent; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications)

RN 666-52-4 HCA

CN 2-Propanone-1,1,1,3,3,3-d6 (9CI) (CA INDEX NAME)

D3C-C-CD3

RN 811-98-3 HCA

CN Methanol-d4 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

D3C-O-D

RN 865-49-6 HCA

CN Methane-d, trichloro- (9CI) (CA INDEX NAME)

C1-C-C1

RN 1076-43-3 HCA

CN Benzene-d6 (8CI, 9CI) (CA INDEX NAME)

$$\begin{array}{c} D \\ D \\ D \end{array}$$

RN 1516-08-1 HCA

CN Ethanol-d6 (9CI) (CA INDEX NAME)

D3C-CD2-O-D

RN 1665-00-5 HCA

CN Methane-d2, dichloro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 1693-74-9 HCA

CN Furan-d4, tetrahydro-d4- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 2037-26-5 HCA

CN Benzene-d5, methyl-d3- (9CI) (CA INDEX NAME)

RN 2206-26-0 HCA

CN Acetonitrile-d3 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 2206-27-1 HCA

CN Methane-d3, sulfinylbis- (9CI) (CA INDEX NAME)

RN 2679-89-2 HCA

CN Ethane-d5, 2,2'-oxybis- (9CI) (CA INDEX NAME)

 $D_3C-CD_2-O-CD_2-CD_3$

RN 4472-41-7 HCA

CN Formamide-1-d, N, N-di(methyl-d3) - (7CI, 8CI, 9CI) (CA INDEX NAME)

RN 7291-22-7 HCA

CN Pyridine-d5 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 7789-20-0 HCA

CN Water-d2 (9CI) (CA INDEX NAME)

D- O- D

RN 17222-37-6 HCA

CN Methane-d3, oxybis- (9CI) (CA INDEX NAME)

D3C-0-CD3

IT **7782-39-0**, Hydrogen-2, uses

(isotope label; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications)

7782-39-0 HCA RN Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME) CN D--- D IC ICM C07K014-195 CC 3-3 (Biochemical Genetics) Section cross-reference(s): 1, 6, 7, 10, 63 ITProteins (10,000-mol.-wt., compn. contg. uracil-DNA glycosylase and; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙΤ Proteins (25,000-mol.-wt., compn. contq. DNA ligase and; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙΤ Proteins (88,000-mol.-wt., compn. contg. Rho factor and; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙT Enzymes, biological studies (DNA gyrases, subunit A, compn. contg. or Rho factor and; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙT Enzymes, biological studies (DNA helicase, RuvA, compn. contg. uracil-DNA glycosylase and; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙT Proteins (FTSA, compn. contg. polynucleotide nucleotidyltransferase and; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙT Molecular chaperones (GroEL, compn. contg. uracil-DNA glycosylase and; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙΤ Heat-shock proteins (HSP 70, compn. contq. polynucleotide nucleotidyltransferase and; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic

acid processing, and drug screening and drug design applications) ΙT Ribosomal proteins (L1, compn. contg. Rho factor and; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙT Ribosomal proteins (L6, compn. contq. uracil-DNA glycosylase and; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙT Ribosomal proteins (S4, compn. contq. ribonucleoside diphosphate reductase and; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙT Infection (bacterial; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙT Antibacterial agents Bioinformatics Cryoprotectants Crystal growth Crystal morphology DNA sequences Drug design Drug screening Exchange reaction Gel electrophoresis Helicobacter pylori Mass spectrometry Molecular cloning NMR (nuclear magnetic resonance) NMR spectroscopy Pathogenic bacteria Protein sequences Pseudomonas aeruginosa Solubility Stability Staphylococcus aureus Streptococcus pneumoniae X-ray diffractometry (cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙT Fusion proteins (chimeric proteins) (cloning, purifn., sequences, and characterization of

(cryoprotectant; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications)

IT Gene, microbial

(dnaN; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications)

IT Elements

(heavy, label; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications)

IT Molecular association

(identification of interacting proteins; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications)

IT Gene, microbial
(lig; cloning, purifn., sequences, and characterization of
polypeptides from pathogenic bacteria involved in nucleic
acid processing, and drug screening and drug design applications)

IT Polyoxyalkylenes, uses

(low-mol.-wt., cryoprotectant; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications)

IT Epitopes

(mapping; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications)

IT Proteins

(mutS, compn. contg. uracil-DNA glycosylase and; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications)

IT Gene, microbial Gene, microbial

(nrdE; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications)

IT Gene, microbial

(nrdF; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications)

ΙT Gene, microbial (pnp; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙT Gene, microbial (pnpA; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙT Organic compounds, biological studies (polypeptides complexed with; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙT Conformation (protein; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙΤ Gene, microbial (pyrE; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙΤ Gene, microbial (pyrH; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙT Gene, microbial (rho; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙΤ Proteins (single-stranded DNA-binding, compn. contg. uracil-DNA glycosylase and; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙΤ Gene, microbial (ung; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙT Genome (virtual genome anal.; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙT Transcription factors (.rho., Staphylococcus aureus; cloning, purifn., sequences, and

characterization of polypeptides from pathogenic

bacteria involved in nucleic acid processing, and drug screening

and drug design applications) ΙT 9030-25-5P, Orotate phosphoribosyltransferase 9036-23-1P, Uridylate kinase (Helicobacter pylori; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) 9012-90-2 9068-08-0, Formate acetyltransferase ΙT (I, compn. contg. Rho factor and; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙT 59088-21-0P, Uracil DNA glycosylase (Pseudomonas aeruginosa; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) 9047-64-7P, Ribonucleoside diphosphate reductase IT (Stahylococcus aureus and S. pneumoniae; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) 9014-12-4P, Polyribonucleotide phosphorylase 455952-24-6P, DNA ΙT (Staphylococcus aureus; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙT 503638-31-1DP, subfragments and variants are claimed 503638-33-3DP, subfragments and variants are claimed 503638-35-5DP, subfragments and variants are claimed 503638-37-7DP, subfragments and variants are claimed 503638-39-9DP, subfragments and variants are claimed 503638-41-3DP, subfragments and variants are claimed 503638-43-5DP, subfragments and variants are claimed 503638-45-7DP, subfragments and variants are claimed 503638-47-9DP, subfragments and variants are claimed 503638-50-4DP, subfragments and variants are claimed 503638-51-5DP, subfragments and variants are claimed (amino acid sequence; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙT 63363-78-0, Endonuclease IV (compn. contg. DNA ligase and; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications)

- ΙT 9014-08-8, Enolase (compn. contg. ribonucleoside diphosphate reductase major subunit and; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and design applications) 9014-24-8, DNA-dependent RNA polymerase ΙT (compn. contq. uracil-DNA glycosylase or Rho factor and; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) 64-18-6, Formic acid, uses ΙT 56-81-5, Glycerol, uses 77-92-9, uses 107-21-1, Ethylene glycol, uses Isopropanol, uses 107-41-5 (cryoprotectant; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΤТ 110-82-7, Cyclohexane, uses **666-52-4**, 2-Propanone-1,1,1,3,3,3-d6 **811-98-3**, Methanol-d4 **865-49-6**, Chloroform-d 1076-43-3, Benzene-d6 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9 2037-26-5 2206-26-0, Acetonitrile-d3 2206-27-1 2679-89-2 4472-41-7, N, N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Heavy water 17222-37-6 (deuterium lock solvent; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) ΙT 433935-36-5P, Polynucleotide nucleotidyl transferase (homolog, Staphylococcus aureus; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) 1333-74-0, Hydrogen, uses 7440-23-5, Sodium-23, uses ITPhosphorus-31, uses 7727-37-9, Nitrogen-14, uses 10028-17-8, Hydrogen-2, uses 7782-41-4, Fluorine-19, uses 14762-74-4, Carbon-13, uses (isotope label; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) 3211-76-5, Selenomethionine 7429-91-6, Dysprosium, uses
- TT 3211-76-5, Selenomethionine 7429-91-6, Dysprosium, uses 7439-88-5, Iridium, uses 7439-90-9, Krypton, uses 7439-91-0, Lanthanum, uses 7439-92-1, Lead, uses 7439-94-3, Lutetium, uses 7439-97-6, Mercury, uses 7439-98-7, Molybdenum, uses 7440-00-8, Neodymium, uses 7440-04-2, Osmium, uses 7440-05-3, Palladium,

7440-06-4, Platinum, uses 7440-10-0, Praseodymium, uses 7440-15-5, Rhenium, uses 7440-16-6, Rhodium, uses 7440-22-4, Silver, 7440-19-9, Samarium, uses Ruthenium, uses 7440-24-6, Strontium, uses 7440-25-7, Tantalum, uses 7440-27-9, Terbium, uses 7440-28-0, Thallium, uses 7440-29-1, 7440-30-4, Thulium, uses 7440-31-5, Tin, uses Thorium, uses 7440-33-7, Tungsten, uses 7440-39-3, Barium, uses 7440-43-9, 7440-45-1, Cerium, uses 7440-48-4, Cobalt, uses Cadmium, uses 7440-53-1, Europium, uses 7440-54-2, 7440-52-0, Erbium, uses Gadolinium, uses 7440-57-5, Gold, uses 7440-60-0, Holmium, uses 7440-61-1, Uranium, uses 7440-63-3, Xenon, uses 7440-64-4, 7553-56-2, Iodine, uses 7726-95-6, Bromine, uses Ytterbium, uses 7782-49-2, Selenium, uses

(label; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications) 25322-68-3, Polyethylene glycol

(low-mol.-wt., cryoprotectant; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications)

IT 59-67-6D, Nicotinic acid, derivs. 621-82-9D, Cinnamic acid, derivs.

(mass spectrometric matrix; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications)

503638-30-0D, DNA (Staphylococcus aureus gene nrdE), subfragments 503638-32-2D, DNA (Helicobacter pylori and variants are claimed gene pyrH), subfragments and variants are claimed 503638-34-4D, DNA (Staphylococcus aureus gene pnpA), subfragments and variants are 503638-36-6D, DNA (Pseudomonas aeruginosa gene ung), 503638-38-8D, DNA subfragments and variants are claimed (Staphylococcus aureus gene rho), subfragments and variants are 503638-40-2D, subfragments and variants are claimed 503638-42-4D, DNA (Helicobacter pylori gene pyrE), subfragments and 503638-44-6D, DNA (Staphylococcus aureus gene variants are claimed lig), subfragments and variants are claimed 503638-46-8D, DNA (Staphylococcus aureus gene dnaN), subfragments and variants are 503638-48-0D, DNA (Staphylococcus aureus gene nrdF), subfragments and variants are claimed 503638-49-1D, DNA (Streptococcus pneumoniae gene nrdE), subfragments and variants are claimed

(nucleotide sequence; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications)

IT 1406-83-3, Leukocidin

ΙT

ΙT

```
(precursor, subunit F, compn. contg. ribonucleoside diphosphate
         reductase and; cloning, sequences, and characterization of
         polypeptides from pathogenic bacteria involved in nucleic
         acid processing, and drug screening and design applications)
ΙΤ
     503643-52-5
                    503643-54-7
                                   503643-55-8
                                                 503643-57-0
                                                                503643-59-2
     503643-60-5
                    503643-61-6
                                   503643-62-7
                                                 503643-63-8
                                                                503643-64-9
     503643-65-0
                    503643-67-2
                                  503643-68-3
                                                 503643-69-4
                                                                503643-71-8
     503643-72-9
                    503643-73-0
                                   503643-75-2
                                                 503643-76-3
                                                                503643-78-5
     503643-80-9
                    503643-81-0
                                  503643-82-1
                                                 503643-84-3
                                                                503643-85-4
     503643-86-5
                    503643-88-7
                                  503643-89-8
                                                 503643-90-1
                                                                503643-92-3
     503643-93-4
         (unclaimed nucleotide sequence; cloning, purifn. and
        characterization of polypeptides from pathogenic
        bacteria involved in nucleic acid processing and drug screening
        and drug design applications)
ΙT
     503643-53-6
                    503643-56-9
                                  503643-58-1
                                                 503643-66-1
                                                                503643-70-7
     503643-74-1
                    503643-77-4
                                  503643-79-6
                                                 503643-83-2
                                                                503643-87-6
     503643-91-2
         (unclaimed protein sequence; cloning, purifn. and
        characterization of polypeptides from pathogenic
        bacteria involved in nucleic acid processing and drug screening
        and drug design applications)
ΙT
     503607-95-2
                    503607-96-3
                                  503607-97-4
                                                 503607-98-5
                                                               503607-99-6
     503608-00-2
                    503608-01-3
                                  503608-02-4
                                                 503608-03-5
                                                               503608-04-6
     503608-05-7
                    503608-06-8
                                  503608-07-9
                                                 503608-08-0
                                                               503608-09-1
     503608-10-4
                    503608-11-5
                                  503608-12-6
                                                 503608-13-7
                                                               503608-14-8
     503608-15-9
                    503608-16-0
                                  503608-17-1
                                                 503608-18-2
                                                               503608-19-3
     503608-20-6
                    503608-21-7
                                  503608-22-8
                                                 503608-23-9
                                                               503608-24-0
     503608-25-1
                    503608-26-2
                                                 503608-28-4
                                  503608-27-3
                                                               503608-29-5
     503608-30-8
                    503608-31-9
                                  503608-32-0
                                                 503608-33-1
                                                               503608-34-2
     503608-35-3
                    503608-36-4
                                  503608-37-5
                                                 503608-38-6
                                                               503608-39-7
     503608-40-0
                                  503608-42-2
                    503608-41-1
                                                 503608-43-3
                                                               503608-44-4
     503608-45-5
                    503608-46-6
                                  503608-47-7
                                                 503608-48-8
                                                               503608-49-9
     503608-50-2
                    503608-51-3
                                  503608-52-4
                                                 503608-53-5
                                                               503608-54-6
     503608-55-7
                    503608-56-8
                                  503608-57-9
                                                 503608-58-0
                                                               503608-59-1
     503608-60-4
                    503608-61-5
                                  503608-62-6
                                                               503608-66-0
                                                 503608-64-8
     503608-67-1
                    503608-68-2
                                  503608-69-3
                                                 503608-70-6
                                                               503608-71-7
     503608-72-8
                    503608-73-9
                                  503608-74-0
                                                 503608-75-1
                                                               503608-76-2
     503608-77-3
                    503608-78-4
                                  503608-79-5
                                                 503608-80-8
                                                               503608-81-9
     503608-82-0
                    503608-83-1
                                  503608-84-2
                                                 503608-85-3
                                                               503608-86-4
     503608-87-5
                    503608-88-6
                                  503608-89-7
                                                 503608-90-0
                                                               503608-91-1
     503608-92-2
                    503608-93-3
                                  503608-94-4
                                                 503608-95-5
                                                               503608-96-6
     503608-97-7
                    503608-98-8
                                  503608-99-9
                                                 503609-00-5
                                                               503609-01-6
     503609-02-7
                    503609-03-8
                                  503609-04-9
                                                 503609-05-0
                                                               503609-06-1
        (unclaimed sequence; cloning, purifn. and characterization of
        polypeptides from pathogenic bacteria involved in nucleic
        acid processing and drug screening and drug design applications)
ΤT
     37217-33-7P, DNA polymerase III
```

(.beta.-subunit, Staphylococcus aureus; cloning, purifn., sequences, and characterization of polypeptides from pathogenic bacteria involved in nucleic acid processing, and drug screening and drug design applications)

L101 ANSWER 18 OF 28 HCA COPYRIGHT 2004 ACS on STN 138:267686 Purification of enzymes involved in coenzyme metabolism from pathogenic bacteria for characterization in development of targets for antibiotics. Edwards, Aled; Dharamsi, Akil; Vedadi, Masoud; Alam, Muhammad Zahoor; Awrey, Donald; Beattie, Bryan; Canadien, Veronica; Domagala, Megan; Houston, Simon; Kanagarajah, Dhushy; Li, Qin; Necakov, Sasha; Nethery, Kathleen; Pinder, Benjamin; Sheldrick, Bay; Vallee, Francois; Viola, Cristina (Affinium Pharmaceuticals, Inc., Can.). PCT Int. Appl. WO 2003025006 A2 20030327, 256 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, (English). CODEN: PIXXD2. APPLICATION: WO 2002-CA1427 20020920. PRIORITY: US 2001-PV324115 20010921; US 2001-PV325337 20010927; US 2001-PV326321 20011001; US 2001-PV326378 20011001; US 2001-PV326820 20011003; US 2001-PV335702 20011025; US 2001-PV340536 20011026; US 2001-PV350907 20011029. Methods of purifying and characterizing enzymes that may play a role AB in cofactor metab. in pathogenic bacteria are described. proteins may be useful as targets for antibiotics and methods for identifying regions of the proteins that may be targeted by drugs are described. The invention also provides biochem. and biophys. characteristics of those polypeptides. 666-52-4, Perdeuteroacetone 811-98-3, Methanol-d4 ΙΤ 865-49-6, Deuterochloroform 1076-43-3, Perdeuterobenzene 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9, Perdeuterotetrahydrofuran 2037-26-5 2206-26-0, Perdeuteroacetonitrile 2206-27-1, Dimethylsulfoxide-d6 2679-89-2, Diethyl ether-d10 4472-41-7, N, N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Heavy water 17222-37-6 (as deuterium lock solvent in NMR of proteins; purifn. of enzymes involved in coenzyme metab. from pathogenic bacteria for characterization in development of targets for antibiotics)

RN 666-52-4 HCA CN 2-Propanone-1,1,1,3,3,3-d6 (9CI) (CA INDEX NAME)

RN 811-98-3 HCA

CN Methanol-d4 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

D3C-O-D

RN 865-49-6 HCA

CN Methane-d, trichloro- (9CI) (CA INDEX NAME)

RN 1076-43-3 HCA

CN Benzene-d6 (8CI, 9CI) (CA INDEX NAME)

$$D \qquad D \qquad D$$

RN 1516-08-1 HCA

CN Ethanol-d6 (9CI) (CA INDEX NAME)

D3C-CD2-O-D

RN 1665-00-5 HCA

CN Methane-d2, dichloro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 1693-74-9 HCA

CN Furan-d4, tetrahydro-d4- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 2037-26-5 HCA

CN Benzene-d5, methyl-d3- (9CI) (CA INDEX NAME)

RN 2206-26-0 HCA

CN Acetonitrile-d3 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 2206-27-1 HCA

CN Methane-d3, sulfinylbis- (9CI) (CA INDEX NAME)

RN 2679-89-2 HCA

CN Ethane-d5, 2,2'-oxybis- (9CI) (CA INDEX NAME)

D3C-CD2-O-CD2-CD3

RN 4472-41-7 HCA

CN Formamide-1-d, N, N-di(methyl-d3) - (7CI, 8CI, 9CI) (CA INDEX NAME)

RN 7291-22-7 HCA

CN Pyridine-d5 (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 7789-20-0 HCA

CN Water-d2 (9CI) (CA INDEX NAME)

D- O- D

RN 17222-37-6 HCA

CN Methane-d3, oxybis- (9CI) (CA INDEX NAME)

D3C-0-CD3

TT 7782-39-0, Deuterium, biological studies
 (as isotopic label for NMR of proteins; purifn. of
 enzymes involved in coenzyme metab. from pathogenic bacteria for
 characterization in development of targets for antibiotics)

RN 7782-39-0 HCA

CN Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME) D-- D IC ICM C07K014-195 CC 7-2 (Enzymes) Section cross-reference(s): 1, 3, 6, 16 ST enzyme purifn NMR mass spectrometry genomics; coenzyme biosynthesis enzyme antibiotic design selection ΙT Hydrocarbon oils Polyoxyalkylenes, biological studies (as cryoprotectant; purifn. of enzymes involved in coenzyme metab. from pathogenic bacteria for characterization in development of targets for antibiotics) ΙΤ NMR spectroscopy (deuterium; purifn. of enzymes involved in coenzyme metab. from pathogenic bacteria for characterization in development of targets for antibiotics) ΙT Crystallization Mass spectrometry (of proteins; purifn. of enzymes involved in coenzyme metab. from pathogenic bacteria for characterization in development of targets for antibiotics) ΙT 56-81-5, Glycerol, biological studies 64-18-6, Formic acid, biological studies 67-63-0, Isopropanol, biological studies 77-92-9, Citric acid, biological studies 107-21-1, Ethylene glycol, biological studies 5683-44-3, 3-Methyl-2,4-pentanediol 25322-68-3, Polyethylene glycol (as cryoprotectant; purifn. of enzymes involved in coenzyme metab. from pathogenic bacteria for characterization in development of targets for antibiotics) ΙT 110-82-7, Cyclohexane, analysis **666-52-4**, Perdeuteroacetone 811-98-3, Methanol-d4 865-49-6 , Deuterochloroform 1076-43-3, Perdeuterobenzene 1516-08-1, Ethanol-d6 1665-00-5 1693-74-9 , Perdeuterotetrahydrofuran 2037-26-5 2206-26-0, Perdeuteroacetonitrile 2206-27-1, Dimethylsulfoxide-d6 2679-89-2, Diethyl ether-d10 4472-41-7, N, N-Dimethylformamide-d7 7291-22-7, Pyridine-d5 7789-20-0, Heavy water 17222-37-6 (as deuterium lock solvent in NMR of proteins; purifn. of enzymes involved in coenzyme metab. from pathogenic bacteria for characterization in development of targets for antibiotics) 7440-23-5, Sodium-23, ΙT 1333-74-0, Hydrogen, biological studies

biological studies 7723-14-0, Phosphorus-31, biological studies

7727-37-9, Nitrogen 14, biological studies **7782-39-0**, **Deuterium**, biological studies 7782-41-4, Fluorine-19,

biological studies 10028-17-8, Tritium, biological studies 14390-96-6, Nitrogen 15, biological studies 14762-74-4, Carbon 13, biological studies

(as isotopic label for NMR of proteins; purifn. of enzymes involved in coenzyme metab. from pathogenic bacteria for characterization in development of targets for antibiotics)

L101 ANSWER 19 OF 28 HCA COPYRIGHT 2004 ACS on STN 138:182010 Nucleic acid sensor molecules comprising target modulation domains and catalytic domains with an optical signal generating Stanton, Martin; Epstein, David; Hamaguchi, Nobuko; Kurz, Markus; Keefe, Tony; Wilson, Charles; Grate, Dilara; Marshall, Kristin A.; McCauley, Thomas; Kurz, Jeffrey (Archemix Corp., USA). PCT Int. Appl. WO 2003014375 A2 20030220, 424 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US25319 20020809. PRIORITY: US 2001-PV311378 20010809; US 2001-PV313932 20010821; US 2001-952680 20010913; US 2001-PV338186 20011113; US 2002-PV349959 20020118; US 2002-PV364486 20020313; US 2002-PV367991 20020325; US 2002-PV369887 20020404; US 2002-PV376744 20020501; US 2002-PV385097 20020531.

Methods for engineering a nucleic acid sensor mol. (also known as AB allosteric ribozymes, aptazymes, and the like) are provided. Biosensors comprise a plurality of nucleic acid sensor mols. labeled with a first signaling moiety and a second signaling moiety. nucleic acid sensor mols. recognizes target mols. which do not naturally bind to DNA. Binding of a target mol. to the sensor mols. triggers a change in the proximity of the signaling moieties which leads to a change in the optical properties of the nucleic acid sensor mols. on the biosensor. The nucleic acid sensor mols. are developed through a combination of engineering and selection methods that are useful for identifying nucleic acid sensor mols. against a wide variety of target mols. including protein (including specific post-translationally modified forms of proteins), peptides , nucleic acids, oligosaccharides, nucleotides, metabolites, drugs, toxins, biohazards, ions, carbohydrates, glycoproteins, hormones, receptors, antibodies, viruses, transition state analogs, cofactors, dyes, growth factors, nutrients, etc. The selection process identified novel sensor mols. through target modulation of the catalytic core of a ribozyme. Hence, in vitro selection is distinct from previously described for affinity-based aptamer selections

(e.g., SELEX) in that selective pressure on the starting population of nucleic acid sensors results in mols. with enhanced catalytic properties, but not in enhanced binding properties. In one embodiment of the invention, nucleic acid sensors are based on cis-cleaving hammerhead ribozymes that have been designed to work as optical signaling mols. affixed to a solid support, and utilize fluorescence and FRET-based methods of signal generation and detection. The method is useful in diagnostic applications and drug optimization.

IT 52-90-4, L-Cysteine, biological studies

(acylation, detection of proteins modified by; nucleic acid sensor mols. comprising target modulation domains and catalytic domains with an optical signal generating unit)

RN 52-90-4 HCA

CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IC ICM C120

CC 3-1 (Biochemical Genetics)

Section cross-reference(s): 1, 7, 9

IT Proteins

(GTP-binding, detection of; nucleic acid sensor mols. comprising target modulation domains and catalytic domains with an optical signal generating unit)

IT Phosphatidylinositols

(addn. of, detection of proteins modified by;

nucleic acid sensor mols. comprising target modulation domains and catalytic domains with an optical signal generating unit)

IT Alkylation

(biochem., detection of proteins modified by;

nucleic acid sensor mols. comprising target modulation domains and catalytic domains with an optical signal generating unit)

IT Acetylation

Acylation

Glycosylation

(biol., detection of proteins modified by;

nucleic acid sensor mols. comprising target modulation domains and catalytic domains with an optical signal generating unit)

IT Deamination

(biol., of asparagine, detection of proteins

modified by; nucleic acid sensor mols. comprising target modulation domains and catalytic domains with an optical signal generating unit) ΙΤ Carboxylation (biol., of glutamine, detection of proteins modified by; nucleic acid sensor mols. comprising target modulation domains and catalytic domains with an optical signal generating unit) ΙT Hydroxylation (biol., of proline, detection of proteins modified by; nucleic acid sensor mols. comprising target modulation domains and catalytic domains with an optical signal generating unit) ΙT Myristoylation Prenylation (detection of proteins modified by; nucleic acid sensor mols. comprising target modulation domains and catalytic domains with an optical signal generating unit) ΤТ Lipids, biological studies (detection of proteins modified by; nucleic acid sensor mols. comprising target modulation domains and catalytic domains with an optical signal generating unit) TΤ Cytokines Estrogen receptors G protein-coupled receptors G proteins (quanine nucleotide-binding proteins) (detection of; nucleic acid sensor mols. comprising target modulation domains and catalytic domains with an optical signal generating unit) ΙT Disulfide group (formation, detection of proteins modified by; nucleic acid sensor mols. comprising target modulation domains and catalytic domains with an optical signal generating unit) ITBiosensors Blood analysis Drug screening Drugs Dyes Fluorescence Fluorescence quenching Fluorescence resonance energy transfer Fluorescent indicators High throughput screening Ions Isotope indicators Nucleic acid hybridization

Nutrients

Surface plasmon resonance

Virus

(nucleic acid sensor mols. comprising target modulation domains and catalytic domains with an optical signal generating unit)

IT Antibodies

Antigens

Carbohydrates, analysis

Coenzymes

Growth factors, animal

Hormones, animal, analysis

Nucleotides, analysis

Oligosaccharides, analysis

Peptides, analysis

Polysaccharides, analysis

Proteins

Receptors

Toxins

(nucleic acid **sensor** mols. comprising target modulation domains and catalytic domains with an optical signal generating unit)

IT Phosphorylation, biological

(protein, detection of proteins

modified by; nucleic acid sensor mols. comprising target modulation domains and catalytic domains with an optical signal generating unit)

- TT 70-47-3, L-Asparagine, biological studies (deamination, detection of proteins modified by; nucleic acid sensor mols. comprising target modulation domains and catalytic domains with an optical signal generating unit)
- IT 60-92-4, CAMP 3616-08-8, CCMP 7665-99-8, CGMP 9001-63-2, Lysozyme 9013-05-2, Phosphatase 9036-21-9, CAMP phosphodiesterase 9068-52-4, CGMP phosphodiesterase 103171-49-9,

Ras kinase 137632-07-6, ERK1 kinase 137632-08-7, ERK2 kinase 139691-76-2, RAF kinase 142243-02-5, ERK kinase 142243-02-5D, ERK kinase, phosphorylated 142805-58-1, Mitogen-activated protein kinase kinase 146702-84-3D, MEK kinase, phosphorylated 155215-87-5, JNK kinase 165245-96-5, p38 MAP kinase 372092-80-3, Protein kinase (detection of; nucleic acid sensor mols. comprising

(detection of; nucleic acid sensor mols. comprising target modulation domains and catalytic domains with an optical signal generating unit)

- 17 10028-17-8, Tritium, uses 14158-31-7, Iodine-125, uses 14596-37-3, Phosphorus-32, uses 14762-75-5, Carbon-14, uses 15117-53-0, Sulfur-35, uses 15749-66-3, Phosphorus-33, uses (radioactive label for sensor; nucleic acid sensor mols. comprising target modulation domains and catalytic domains with an optical signal generating unit)
- IT 63-68-3, L-Methionine, biological studies
 (removal of, detection of proteins modified
 by; nucleic acid sensor mols. comprising target modulation
 domains and catalytic domains with an optical signal generating
 unit)
- L101 ANSWER 20 OF 28 HCA COPYRIGHT 2004 ACS on STN
 137:197868 Phosphoprotein binding agents and methods of their use.
 Goshe, Michael B.; Conrads, Thomas P.; Veenstra, Timothy D.;
 Panisko, Ellen A. (USA). U.S. Pat. Appl. Publ. US 2002119505 A1
 20020829, 20 pp. (English). CODEN: USXXCO. APPLICATION: US
 2001-788286 20010216.
- AΒ The invention provides reagents and methods for characterizing (i.e., identification and/or quantitation) the phosphorylation states of proteins. Proteins may be post-transcriptionally modified such that they contain phosphate groups at either some or all of their serine, threonine, tyrosine, histidine, and/or lysine amino acid residues. In many cases the extent to which a protein is phosphorylated dets. its bioactivity, i.e., its ability to effect cell functions such as differentiation, division, and metab. Hence, a powerful tool for diagnosing various diseases and for furthering the understanding of protein-protein interactions is Two equal .beta.-casein samples were labeled with ethanedithiol (EDT) or EDT-2H4, resp., under .beta.-elimination conditions with NaOH. The labeled samples were quenched, desalted, denatured, reduced, biotinylated with iodoacetyl-PEO -biotin, and digested with trypsin. The labeled peptides were purified by affinity chromatog. using

```
immobilized avidin and analyzed capillary reversed-phase liq.
     chromatog.-mass spectrometry.
ΙT
     7782-39-0, 2H, uses
        (as label; phosphoprotein binding agents and methods of use)
RN
     7782-39-0 HCA
CN
     Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME)
D— D
ΙT
     100189-81-9, 1,2-Ethane-1,1,2,2-d4-dithiol
        (phosphoprotein binding agents and methods of use)
RN
     100189-81-9 HCA
CN
     1,2-Ethane-1,1,2,2-d4-dithiol (9CI) (CA INDEX NAME)
HS-CD2-CD2-SH
IC
     ICM G01N033-537
     ICS G01N033-543
NCL
     435007920
CC
     9-16 (Biochemical Methods)
     Section cross-reference(s): 6
     phosphoprotein phosphorylation analysis reagent; diagnosis
ST
     phosphoprotein binding agent; protein interaction study
     phosphoprotein binding agent; beta casein phosphopeptide labeling
     deuterated ethandithiol; affinity chromatog mass
     spectrometry phosphopeptide identification
ΙT
     Isotopes
        (as labels; phosphoprotein binding agents and methods of use)
ΙT
     Protein sequence analysis
        (mass spectrometric; phosphoprotein binding
        agents and methods of use)
IT
     Amino acids, analysis
        (phosphates, protein contg.; phosphoprotein binding
        agents and methods of use)
ΙT
     Affinity chromatography
     Cell
     Cell differentiation
     Cell division
    Chromatography
     Coupling agents
     Diagnosis
     Disease, animal
    Metabolism
    Metabolism, animal
     Phosphate group
     Samples
```

```
(phosphoprotein binding agents and methods of use)
ΙT
     Peptides, analysis
        (phosphoprotein binding agents and methods of use)
ΙT
     Mass spectrometry
        (protein sequence anal.; phosphoprotein
        binding agents and methods of use)
                           13965-97-4, 34S, uses 13968-48-4,
     7782-39-0, 2H, uses
IT
     170, uses 14390-96-6, 15N, uses 14762-74-4, 13C, uses
     14797-71-8, 180, uses
        (as label; phosphoprotein binding agents and methods of use)
     540-63-6, 1,2-Ethanedithiol 100189-81-9,
IT.
     1,2-Ethane-1,1,2,2-d4-dithiol
                                     339082-21-2
        (phosphoprotein binding agents and methods of use)
L101 ANSWER 21 OF 28 HCA COPYRIGHT 2004 ACS on STN
136:366141 Method for assaying protein
                     Jaffrey, Samie; Ferris, Christopher D.; Snyder,
     nitrosylation.
     Solomon H. (The Johns Hopkins University, USA; Memorial
     Sloan-Kettering Cancer Center; Erdjument-Bromage, Hediye; Tempst,
    Paul). PCT Int. Appl. WO 2002039119 A2 20020516, 39 pp. DESIGNATED
     STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,
     CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE,
    GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
     LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
     PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
    UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE,
     BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE,
    IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English).
     CODEN: PIXXD2. APPLICATION: WO 2001-US42826 20011029. PRIORITY: US
     2000-PV244097 20001027.
    Many of the effects of nitric oxide are mediated by the direct
AB
     modification of cysteine residues resulting in an adduct
     called a nitrosothiol. A method to detect
     proteins which contain nitrosothiols involves several steps.
     Nitrosylated cysteines are converted to tagged
     cysteines. Tagged proteins can then be detected, for
     example, by immunoblotting and/or can be purified by affinity
     chromatog. The method is applicable to the detection of
     S-nitrosylated proteins in cell lysates following in vitro
     S-nitrosylation, as well as to the detection of endogenous
     S-nitrosothiols in selected protein substrates.
     52-90-4, L-Cysteine, biological studies
IT
        (method for assaying protein nitrosylation)
```

Absolute stereochemistry.

L-Cysteine (9CI) (CA INDEX NAME)

52-90-4 HCA

RN

CN

Tandem mass spectrometry

```
NH2
               SH
IC
```

ICM G01N033-68

9-14 (Biochemical Methods) CC

Section cross-reference(s): 6

protein nitrosylation assay nitrosothiol ST

ΙT Heat-shock proteins

(HSP 72; method for assaying protein

nitrosylation)

ΙT Neurofilament proteins

(NF-H; method for assaying protein

nitrosylation)

ΙT Glutamate receptors

> (NMDA-binding, NR1 or NR2 subunits; method for assaying protein nitrosylation)

ΙT Transcription factors

(Rb; method for assaying protein

nitrosylation)

ΙΤ Radioactive substances

(as label on activated mixed disulfide;

method for assaying protein nitrosylation)

Peptides, biological studies IT

(as label on activated mixed disulfide; method for

assaying protein nitrosylation)

ΙT Proteins

(collapsin response mediator protein 1; method for

assaying protein nitrosylation)

ΙΤ Proteins

(collapsin response mediator protein 2; method for

assaying protein nitrosylation)

ΙΤ Proteins

(collapsin response mediator protein 4; method for

assaying protein nitrosylation)

ΙT

(detectably tagged and activated mixed; method for

assaying protein nitrosylation)

ΙT Drug screening

(for drugs modulating protein nitrosylation; method for

assaying protein nitrosylation)

Cation channel ΙT

(hyperpolarization-activated, isoform 2 or 3 of; method for

assaying protein nitrosylation)

ΙT Immunoassay

(immunoblotting; method for assaying protein nitrosylation) IΤ Affinity chromatography Nitrosation Test kits (method for assaying protein nitrosylation) ΙΤ Antibodies Avidins (method for assaying protein nitrosylation) ΙT Calbindins (method for assaying protein nitrosylation) IΤ Thiols (organic), biological studies (method for assaying protein nitrosylation) ITProteins (nitrosylated; method for assaying protein nitrosylation) TΤ Blood vessel Brain Macrophage (test sample from; method for assaying protein nitrosylation) ITNitrosation (thionitrosation; method for assaying protein nitrosylation) ΙΤ Tubulins (.alpha.-; method for assaying protein nitrosylation) ΙT Actins Tubulins (.beta.-; method for assaying protein nitrosylation) ΙT Actins (.gamma.-; method for assaying protein nitrosylation) ΙT 58-85-5, Biotin 25550-58-7, Dinitrophenol (as label on activated mixed disulfide; method for assaying protein nitrosylation) ΙT 125978-95-2, Nitric oxide synthetase (endothelial and neuronal; method for assaying protein nitrosylation) 9001-51-8, Hexokinase IT (isoform 1; method for assaying protein nitrosylation) IΤ 9013-20-1, Streptavidin (method for assaying protein nitrosylation) ΙT 9001-15-4, Creatine kinase 9001-50-7, Glyceraldehyde-3-phosphate dehydrogenase 9035-74-9, Glycogen phosphorylase (method for assaying protein nitrosylation)

Wallenhorst 10/045,170

IT 52-90-4, L-Cysteine, biological studies

(method for assaying protein nitrosylation)

IT 50-81-7, L-Ascorbic acid, uses 67-64-1, Acetone, uses 134-5. Sodium ascorbate 151-21-3, SDS, uses

(method for assaying protein nitrosylation)

IT 2949-92-0 3614-08-2, Selenocysteine 15537-71-0, N-Acetylpenicillamine 67776-06-1, S-Nitrosoacetylpenicillamine 129179-83-5

(method for assaying protein nitrosylation)

IT 9000-83-3

(potassium-sodium-dependent, .alpha.1 or .alpha.2 subunit; method for assaying protein nitrosylation)

- L101 ANSWER 22 OF 28 HCA COPYRIGHT 2004 ACS on STN
- 134:307611 Conjugated polymer tag complexes and their preparation and use in assays. Leif, Robert C.; Franson, Richard C.; Vallarino, Lidia (USA). PCT Int. Appl. WO 2001027625 A1 20010419, 104 pp. DESIGNATED STATES: W: CA, CH, DE, FI, GB, JP, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US27787 20001007. PRIORITY: US 1999-PV158718 19991008.
- Processes are described for: (1) the sequential solid phase AΒ synthesis of polymers with at least one tag, which can be a light emitting and/or absorbing mol. species (optical-label), a paramagnetic or radioactive label, or a tag that permits the phys. sepn. of particles including cells. When multiple optical-labels are suitably arranged in three-dimensional space, the energy transfer from one mol. species to another can be maximized and the radiationless loss between members of the same mol. species can be minimized; (2) the coupling of these polymers to biol. active and/or biol. compatible mols. through peripheral pendant substituents having at least one reactive site; and (3) the specific cleavage of the coupled polymer from a solid phase support. tagged-peptide or polymers produced by these processes and their conjugates with an analyte-binding species, such as a monoclonal antibody or a polynucleotide probe are described. functionalized europium macrocyclic complexes, as taught in our U.S. patents 5,373,093 and 5,696,240, are bound to polylysine and other peptides, the emitted light increases linearly with the amt. of bound macrocyclic complex. Similar linearity will also result for multiple luminescent macrocyclic complexes of other lanthanide ions, such as samarium, terbium, and dysprosium, when they are bound to a polymer or mol.
- IT 52-90-4, L-Cysteine, biological studies

(conjugated polymer tag complexes and prepn. and use in assays)

- RN 52-90-4 HCA
- CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Nucleosome

Optical absorption

```
NH2
            SH
IC
     ICM G01N033-545
     ICS G01N033-543; G01N033-576; G01N033-532; C08F002-10; C08F002-50;
          C08F290-14
     9-15 (Biochemical Methods)
CC
     Section cross-reference(s): 2, 6, 34, 78, 79, 80
     conjugated polymer tag prepn assay reagent peptide
ST
     Paramagnetic materials
ΙT
       Radioactive substances
        (as labels; conjugated polymer tag complexes and prepn.
        and use in assays)
ΙΤ
     Amino group
     Apoptosis
     Azo dyes
     B cell (lymphocyte)
     Bacillus stearothermophilus
     Carboxyl group
     Cell cycle
     Centromeres
     Chromosome
     Combinatorial chemistry
     Conformation
     Cyanine dyes
     Cyano group
       Disulfide group
     Drugs
     Drugs of abuse
     Energy transfer
     Fluorescent indicators
     Fluorescent substances
     Formyl group
     Human immunodeficiency virus
     Human immunodeficiency virus 1
     Hydroxyl group
     Leukocyte
     Luminescence
     Neoplasm
     Nocardia otitidiscaviarum
     Nucleic acid hybridization
```

ΙT

Pesticides Reducing agents Ribosome Solid phase synthesis Stains, biological Sulfhydryl group T cell (lymphocyte) Telomeres (chromosome) (conjugated polymer tag complexes and prepn. and use in assays) Agglutinins and Lectins Albumins, analysis Antigens Avidins Blood-group substances CD20 (antigen) CD4 (antigen) CD8 (antigen) Carcinoembryonic antigen Collagens, analysis Cyclins DNA Ecdysteroids Estrogen receptors Estrogens Globulins, analysis Glucocorticoid receptors Glycoproteins, general, analysis Glycosaminoglycans, analysis Hemoglobins Hormone receptors Hormones, animal, analysis Immunoglobulins Keratins Lymphokines Nucleic acids Nucleosides, analysis P-glycoproteins Peptides, analysis Polynucleotides Polysaccharides, analysis Progesterone receptors Proliferating cell nuclear antigen Prostaglandins Proteins, general, analysis RNA Toxins Viral RNA

Vitamins mRNA neu (receptor) p53 (protein) .alpha.-Fetoproteins

(conjugated polymer tag complexes and prepn. and use in assays)

IT Nucleic acids

Peptides, preparation

Polymers, preparation

(conjugates; conjugated polymer tag complexes and prepn. and use in assays)

IT Peptides, analysis

Steroids, analysis

(hormones; conjugated polymer tag complexes and prepn. and use in assays)

IT **52-90-4,** L-**Cysteine,** biological studies 73-22-3, L-Tryptophan, biological studies 38240-29-8 142939-57-9 335196-03-7

(conjugated polymer tag complexes and prepn. and use in assays)

L101 ANSWER 23 OF 28 HCA COPYRIGHT 2004 ACS on STN

- 119:155015 Protein- and peptide-metal ion complexes for disease diagnosis and therapy. Rhodes, Buck A.; Zamora, Paul O. (Rhomed Inc., USA). PCT Int. Appl. WO 9312819 A1 19930708, 61 pp. DESIGNATED STATES: W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US11334 19921231. PRIORITY: US 1992-816476 19920103; US 1992-816477 19920103; US 1992-840077 19920220; US 1992-998820 19921230; US 1992-998910 19921230.
- AB The title metal/proteins or peptides complexes comprise a biol. function domain (e.g. IKVAV or YIGSR-contg. domain), a metal ion-binding domain (e.g. domain contg. S, N, O, cysteine, penicillamide), and a metal ion label (Fe, Co, Ni, etc.). Thus, 99mTc-labeled H2N-Cys-Asp-Pro-Gly-Tyr-Ile-Gly-Ser-Arg was prepd. by reaction with stannous tartrate, and then radiolabeling with Na99mTcO4. The labeled peptide was used for detecting clots.

RN 52-90-4 HCA

CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

```
NHo
             SH
HO<sub>2</sub>C
IC
     ICM A61K049-02
     ICS A61K043-00; C07K007-00; C07K015-28
CC
     8-9 (Radiation Biochemistry)
ST
     metal protein complex imaging agent; peptide metal complex
     imaging agent; clot imaging protein metal complex; therapeutic
     polypeptide metal complex
ΙΤ
     Abscess
         (detection of occult, protein/peptide
        -metal ion complexes for)
ΙT
     Emphysema
     Inflammation
     Thrombus and Blood clot
         (detection of, protein/peptide
        -metal ion complexes for)
ΙT
     Imaging
         (NMR, protein/peptide-metal complexes for)
ΙT
     Intestine, neoplasm
        (colon, carcinoma, detection of, protein/
        peptide-metal ion complexes for)
ΙΤ
     Proteins, specific or class
        (disulfide-contg., labeling of, by redn./complex
        formation with stannous ion, for disease diagnosis and therapy)
ΙΤ
     Tomography
        (gamma-ray, protein/peptide-metal complexes for)
ΙT
     Lung, neoplasm
        (melanoma, detection of, protein/
        peptide-metal ion complexes for)
ΙT
     Peptides, compounds
        (metal complexes, prepn. of, for disease diagnosis and therapy)
ΙΤ
     Tomography
        (positron-emission, computerized, protein/peptide-metal
        complexes for)
ΙT
     Tomography
        (single-photon-emission, computerized, protein/peptide
        -metal complexes for)
ΙΤ
     22541-90-8, Tin(2+), biological studies
        (agent contg., for redn./complex formation with thiolate-contg.
```

protein, for disease diagnosis and therapy)

7439-88-5D, Iridium, biol. function domain-contg. and metal

7439-89-6D, Iron, biol. function domain-contg. and metal ion-binding

ion-binding domain-contg. protein or peptide complexes

IT

domain-contg. protein or peptide complexes 7439-92-1D. Lead, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7439-97-6D, Mercury, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7439-98-7D, Molybdenum, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7440-02-0D, Nickel, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7440-04-2D, Osmium, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7440-05-3D, Palladium, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7440-06-4D, Platinum, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7440-08-6D, Polonium, biol. function domain-contg. and metal ion-binding domain-contq. protein or peptide complexes 7440-15-5D, Rhenium, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7440-18-8D, Ruthenium, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7440-22-4D, Silver, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7440-26-8D, Technetium, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7440-28-0D, Thallium, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7440-36-0D, Antimony, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7440-38-2D, Arsenic, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7440-43-9D, Cadmium, biol. function domain-contg. and metal ion-binding domain-contg. protein or **peptide** complexes 7440-48-4D, Cobalt, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7440-50-8D, Copper, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7440-57-5D, Gold, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7440-66-6D, Zinc, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7440-68-8D, Astatine, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7440-69-9D, Bismuth, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7440-74-6D, Indium, biol. function domain-contg. and metal ion-binding domain-contg. protein or peptide complexes 7782-49-2D, Selenium, biol. function domain-contg. and metal ion-binding

domain-contg. protein or peptide complexes
 (for disease diagnosis and therapy)

IT 110590-64-2 131167-89-0

(protein or **peptide** contg. biol. function domain fragment of, metal ion complexed with, for disease diagnosis or therapy)

TT 52-67-5, Penicillamine **52-90-4**, **Cysteine**, biological studies 56-84-8, Aspartic acid, biological studies 56-86-0, Glutamic acid, biological studies 56-87-1, Lysine, biological studies 56-89-3, Cystine, biological studies 60-18-4, Tyrosine, biological studies 63-68-3D, Methionine, deacylated 71-00-1, Histidine, biological studies 74-79-3, Arginine, biological studies 7704-34-9, Sulfur, biological studies 7727-37-9, Nitrogen, biological studies 7782-44-7, Oxygen, biological studies

(protein or **peptide** with metal ion-binding domain contg., metal ion complexed with, for disease diagnosis or therapy)

- L101 ANSWER 24 OF 28 HCA COPYRIGHT 2004 ACS on STN
- 109:108666 Evidence for specific association between class I major histocompatibility antigens and the CD8 molecules of human suppressor/cytotoxic cells. Blue, Marie Luise; Craig, Kimberly A.; Anderson, Paul; Branton, Kenneth R., Jr.; Schlossman, Stuart F. (Dana-Farber Cancer Inst., Harvard Med. Sch., Boston, MA, 02115, USA). Cell (Cambridge, MA, United States), 54(3), 413-21 (English) 1988. CODEN: CELLB5. ISSN: 0092-8674.
- Human T lymphocytes, metabolically labeled with 35S-cysteine AΒ and 35S-methionine, were reacted with the bifunctional crosslinking reagent, dithiobis(succinimidylpropionate) (DSP). When detergent lysates from these cells were immunopptd. with a monoclonal antibody reactive with the CD8 antigen, a radiolabeled protein of .apprx.44 kd was copptd. with the CD8 mol. Immunoppts. from detergent lysates prepd. without prior chem. crosslinking contained only the 33 kd CD8 mol. Similar results were obtained when T lymphocytes or a cytotoxic T cell clone were radiolabeled with 32P-orthophosphoric acid. The 44 kd CD8-assocd. protein was identified as the heavy chain of the class I major histocompatibility antigen by depletion in preclearing expts. with anti-class I MHC antibody and by peptide The CD8-class I MHC assocn. is due, in part at least, to disulfide bonding, which may be susceptible to cleavage during processing of cell lysates.
- CC 15-2 (Immunochemistry)
- IT Disulfide group

(of class I histocompatibility antigen-CD8 antigen complexes, of T-suppressor lymphocyte, of human)

L101 ANSWER 25 OF 28 HCA COPYRIGHT 2004 ACS on STN

109:2641 Human tissue factor contains thioester-linked palmitate and stearate on the cytoplasmic half-cystine. Bach, Ronald; Konigsberg, William H.; Nemerson, Yale (Mt. Sinai Sch. Med., City Univ. New York, New York, NY, 10029, USA). Biochemistry, 27(12), 4227-31 (English) 1988. CODEN: BICHAW. ISSN: 0006-2960.

AB The state of the 5 half-cystine residues in human tissue factor (TF) was characterized. The results indicate that the 4 half-cystines in the extracellular domain of TF form 2 ss bonds and the half-cystine in the cytoplasmic region is acylated by palmitic acid and stearic acid. The extracellular SS crosslinks, Cys49-Cys57 and Cys186-Cys209, were deduced from the anal. of tryptic peptides. Acylation of the cytoplasmic half-cystine was demonstrated by purifying and characterizing fibroblast TF from cells labeled with [3H]palmitic acid. Radiolabeled fibroblast TF was obsd. by autoradiog. following SDS-PAGE. The tritiated material covalently bound to the protein was identified as [3H]palmitate and [3H]stearate by reverse-phase HPLC. Deacylation of TF with hydroxylamine resulted in the spontaneous generation of ss -linked TF dimers. This suggests that the SS-linked TF dimer, a minor component of most TF prepns., and the recently described heterodimeric form of TF are artifacts produced by deacylation of cysteine-245 and subsequent interchain SS bond formation.

RN 52-90-4 HCA

CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

CC 6-3 (General Biochemistry)

ST tissue factor cysteine palmitate stearate thioester; blood coagulation factor III cysteine thioester;

disulfide group tissue factor

IT Disulfide group

(of blood-coagulation factor III, of human)

IT 9035-58-9, Blood-coagulation factor III

(cysteine thioesters with palmitate and stearate and

disulfide groups of, of human)

- L101 ANSWER 26 OF 28 HCA COPYRIGHT 2004 ACS on STN 93:64435 Some physicochemical properties of the deamidase AG from Pseudomonas fluorescens AG. Rakov, S. S.; Prozorovskii, V. N.; Grebenshchikova, O. G. (Lab. Enzimol., Moscow, USSR). Probl. Zlokach. Rosta, 75-80. Editor(s): Berezov, T. T. Univ. Druzhby Nar. im. Patrisa Lumumby: Moscow, USSR. (Russian) 1977. CODEN: 43RQA4.
- The amino acid compn. of deamidase AG (I) from P. fluorescens AG was AΒ detd.; 8 residues of carboxymethylcysteine were detected. I was reduced and carboxymethylated with iodoacetic acid-14C and the amt. of radioactivity in the protein Eight mol. iodoacetate-14C were incorporated/mol I. Without previous redn. by dithiothreitol, no iodoacetate-14C was incorporated into I, indicating that the native enzyme contains no free SH groups. Chymotryptic hydrolysis of carboxymethylated I resulted in the formation of only 2 peptides. Apparently, I contains 4 SS bonds and is composed of no less than 4 subunits. The N-terminal amino acid was lysine; no other N-terminal amino acids were found. Electrophoresis of I incubated with SDS in the presence or absence of dithiothreitol or .beta.-mercaptoethanol resulted in the appearance of 2 protein bands, a major band with mol. wt. of 30,000 and a 2nd band with mol. w. of 42,000. contains 4 very similar or identical subunits of mol. wt. 30,000. The subunits of I are not joined by ${\bf ss}$ bonds since I was dissocd. by SDS alone; it is proposed that each subunit of I contains 1 SS bond. I contains .apprx.9% carbohydrate which may account for the 2nd band (42,000) obsd. on electrophoresis.
- CC 7-2 (Enzymes)
- L101 ANSWER 27 OF 28 HCA COPYRIGHT 2004 ACS on STN 83:189816 Subunit structure and amino acid composition of xylose isomerase from Streptomyces albus. Hogue-Angeletti, Ruth A. (Fox Chase Cancer Cent., Inst. Cancer Res., Philadelphia, PA, USA). Journal of Biological Chemistry, 250(19), 7814-18 (English) 1975. CODEN: JBCHA3. ISSN: 0021-9258.
- AB The subunit structure and amino acid compn. of xylose isomerase from S. albus were examd. A native mol. wt. of 165,000 detd. by sedimentation equil. was reduced to 43,000 when the protein was treated with 6M guanidine-HCl. No further redn. in mol. wt. was obsd. when potential SS bridges of xylose isomerase were reduced and alkylated, indicating that the protein

was devoid of interchain SS bonds. N-terminal anal. showed 0.86 residues of methionine/41,500 mol. wt. unit. Fractionation of the sol. tryptic peptides of S-carboxymethyl xylose isomerase by ion exchange chromatog. and 1-dimensional paper electrophoresis yielded 37-43 peptides When the acid-insol. tryptic peptides were dissolved and analyzed by gel filtration techniques, an addnl. 4 peptides were found. A unique radioactive tryptic peptide contg. S-carboxymethylcysteine was found among the sol. peptides, confirming cysteine as the limiting amino acid residue in the amino acid compn. of xylose isomerase. On the basis of its lysine and arginine content, the no. of tryptic peptides is consistent with the hypothesis that the native xylose isomerase is a tetramer of 4 very similar or identical subunits of mol. wt. 41,500, assocd. by noncovalent bonds. 7-5 (Enzymes)

- L101 ANSWER 28 OF 28 HCA COPYRIGHT 2004 ACS on STN 57:58717 Original Reference No. 57:11712e-g Significance of isotope indicators in development of peculiarities of protein metabolism in organs and tissues in various states of the organism. Konikova, A. S. Tr. Tashkentsk. Konf. po Mirnormu Ispol'z. At. Energii, Akad. Nauk Uz. SSR, 3, 33-7 (Unavailable) 1961.
- AB Treatment of myosin with aq. urea to rupture the H bonding of the protein results in a great increase of incorporation of tagged cysteine, while the incorporation of methionine is changed but little and incorporation of tyrosine and esp. glycine are greatly decreased. The effect on albumin is similar. results were obtained with in vivo expts. on rabbit serum proteins and liver proteins, with the animals kept in hypothermic state. In such animals the inclusion of glycine and methionine is retarded and that of cysteine greatly enhanced. Almost all cysteine is bound in this process by strong peptide bonds in liver protein, but in serum protein the main bulk of the amino acid is linked by labile disulfide bonding. normally maintained animals the proportion of disulfide bonding is only 50%. The changes observed in hypothermia are normalized within 4 days under normal temp. The variability of amino acid incorporation is discussed in the light of possible metabolic cycles.
- IT 52-90-4, Cysteine
 - (in protein formation, after urea denaturation, H bonding and)
- RN 52-90-4 HCA

CC

CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

CC 69 (Mammalian Physiological Chemistry)

IT Isotopes

(as indicators, in protein metabolism)

IT Peptides

(bonds of, cysteine binding in proteins of liver by)

IT Disulfide group

(cysteine binding in proteins of blood serum by)

IT Proteins

(metabolism of, isotopes as indicators of)

IT **52-90-4, Cysteine** 56-40-6, Glycine 60-18-4, Tyrosine

(in protein formation, after urea denaturation, H bonding and)

=> d 1102 1-24 ti

L102 ANSWER 1 OF 24 HCA COPYRIGHT 2004 ACS on STN

TI Characterization of the elusive disulfide bridge forming

human Hb variant: Hb Ta-Li .beta.83 (EF7) Gly.fwdarw.Cys by electrospray mass spectrometry

L102 ANSWER 2 OF 24 HCA COPYRIGHT 2004 ACS on STN

TI Identification of a novel heterodimeric outer membrane protein of Porphyromonas gingivalis by two-dimensional gel electrophoresis and peptide mass fingerprinting

L102 ANSWER 3 OF 24 HCA COPYRIGHT 2004 ACS on STN

TI Identification and location of a cysteinyl posttranslational modification in an amyloidogenic .kappa.l light chain protein by electrospray ionization and matrix-assisted laser desorption/ionization mass spectrometry

L102 ANSWER 4 OF 24 HCA COPYRIGHT 2004 ACS on STN

TI Determination of **disulfide** bond assignments and N-glycosylation sites of the human gastrointestinal carcinoma antigen GA733-2 (CO17-1A, EGP, KS1-4, KSA, and Ep-CAM)

L102 ANSWER 5 OF 24 HCA COPYRIGHT 2004 ACS on STN

TI Characterization of cysteine residues and disulfide bonds in proteins by liquid chromatography/electrospray ionization tandem mass spectrometry

- L102 ANSWER 6 OF 24 HCA COPYRIGHT 2004 ACS on STN
- TI Mass spectrometric mapping of disulfide bonds in recombinant human interleukin-13
- L102 ANSWER 7 OF 24 HCA COPYRIGHT 2004 ACS on STN
- TI Development of **Disulfide Peptide** Mapping and Determination of **Disulfide** Structure of Recombinant Human Osteoprotegerin Chimera Produced in Escherichia coli
- L102 ANSWER 8 OF 24 HCA COPYRIGHT 2004 ACS on STN
- TI Albumin Banks Peninsula: a new termination variant characterised by electrospray mass spectrometry
- L102 ANSWER 9 OF 24 HCA COPYRIGHT 2004 ACS on STN
- TI Selective cyanylation of cysteinyl residues as an approach for the mass spectrometric determination of protein structures
- L102 ANSWER 10 OF 24 HCA COPYRIGHT 2004 ACS on STN
- TI Selective bridging of bis-cysteinyl residues by arsonous acid derivatives as an approach to the characterization of protein tertiary structures and folding pathways by mass spectrometry
- L102 ANSWER 11 OF 24 HCA COPYRIGHT 2004 ACS on STN TI Partial amino acid sequence of .gamma.-46 gliadin
- L102 ANSWER 12 OF 24 HCA COPYRIGHT 2004 ACS on STN
 TI Disulfide bond assignment in human interleukin-7 by
 matrix-assisted laser desorption/ionization mass
 spectroscopy and site-directed cysteine to serine
 mutational analysis
- L102 ANSWER 13 OF 24 HCA COPYRIGHT 2004 ACS on STN

 TI Determination of Tumor Necrosis Factor Binding Protein

 Disulfide Structure: Deviation of the Fourth Domain

 Structure from the TNFR/NGFR Family Cysteine-Rich Region

 Signature
- L102 ANSWER 14 OF 24 HCA COPYRIGHT 2004 ACS on STN
 TI Rat liver fatty acid-binding protein:
 identification of a molecular species having a mixed disulfide with cysteine at cysteine-69
 and enhanced protease susceptibility
- L102 ANSWER 15 OF 24 HCA COPYRIGHT 2004 ACS on STN
- TI Assignment of protein disulfides by a computer method

using mass spectrometric data

- L102 ANSWER 16 OF 24 HCA COPYRIGHT 2004 ACS on STN
- TI **Disulfide** bonds of herpes simplex virus type 2 glycoprotein gB
- L102 ANSWER 17 OF 24 HCA COPYRIGHT 2004 ACS on STN
- TI S-Pyridylethylation of intact polyacrylamide gels and in situ digestion of electrophoretically separated proteins: a rapid mass spectrometric method for identifying cysteine-containing peptides
- L102 ANSWER 18 OF 24 HCA COPYRIGHT 2004 ACS on STN
- TI Cataloguing post-translational modifications of the scrapie prion protein by mass spectrometry
- L102 ANSWER 19 OF 24 HCA COPYRIGHT 2004 ACS on STN
- Isolation and characterization of a resistant core **peptide** of recombinant human granulocyte-macrophage colony-stimulating factor (GM-CSF); Confirmation of the GM-CSF amino acid sequence by mass spectrometry
- L102 ANSWER 20 OF 24 HCA COPYRIGHT 2004 ACS on STN
- TI Characterization of a mixture of lobster digestive cysteine proteinases by ionspray mass spectrometry and tryptic mapping with LC-MS and LC-MS-MS
- L102 ANSWER 21 OF 24 HCA COPYRIGHT 2004 ACS on STN
- Mass spectrometric analysis of the structure of .gamma.II bovine lens crystallin
- L102 ANSWER 22 OF 24 HCA COPYRIGHT 2004 ACS on STN
- TI Strategies for determination of **disulfide** bridges in proteins using plasma desorption **mass spectrometry**
- L102 ANSWER 23 OF 24 HCA COPYRIGHT 2004 ACS on STN
- TI **Disulfide** bond assignment in human tissue inhibitor of metalloproteinases (TIMP)
- L102 ANSWER 24 OF 24 HCA COPYRIGHT 2004 ACS on STN
- TI Verification by mass spectrometry of the primary structure of human interleukin-2
- => d 1102 1,4,5,6,17,22 cbib abs hitstr hitind
- L102 ANSWER 1 OF 24 HCA COPYRIGHT 2004 ACS on STN

136:212513 Characterization of the elusive disulfide bridge forming human Hb variant: Hb Ta-Li .beta.83 (EF7) Gly.fwdarw.Cys by electrospray mass spectrometry. Rai, Dilip K.; Landin, Britta; Griffiths, William J.; Alvelius, Gunvor; Green, Brian N. (Department of Medical Laboratory Sciences and Technology, Division of Clinical Chemistry, Huddinge University Hospital, Karolinska Institutet, Stockholm, Swed.). Journal of the American Society for Mass Spectrometry, 13(2), 187-191 (English) 2002. CODEN: JAMSEF. ISSN: 1044-0305. Publisher: Elsevier Science Inc..

AΒ An electrospray mass spectrometric approach to the identification of a human Hb variant involving a Cys residue incorporation is presented. In Hb Ta-Li (.beta.83Gly .fwdarw. Cys), Cys83 forms intermol. disulfide bridges. Routine anal. of the denatured Hb showed the presence of a minor .beta. chain variant whose mass apparently was 1 Da less than the expected mass difference of 46 Da for a Gly .fwdarw. Cys substitution. Redn. of the globin chains with dithiothreitol gave an intense monomer with the expected mass difference for the Gly .fwdarw. Cys substitution. After reprocessing the original raw data from the denatured Hb and taking into account the possibility of dimer formation, a component was revealed whose mass was consistent with a disulfide -linked dimer of Ta-Li .beta. globins. The mutation was localized to peptide .beta.T10 by anal. of a tryptic digest

. Tandem mass spectrometry and DNA sequencing confirmed the Gly .fwdarw. Cys substitution occurred at residue 83 of the .beta. chain. Problems encountered in identifying the components in mixts. of monomers and dimers are discussed.

IT 52-90-4, L-Cysteine, properties

(electrospray mass spectrometry permits characterization of disulfide bridge-forming human Hb variant Ta-Li (.beta.83Gly.fwdarw.Cys))

RN 52-90-4 HCA

CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

CC 6-3 (General Biochemistry)
Section cross-reference(s): 9

ST Hb cysteine mutation disulfide bridge mass spectrometry

IT Hemoglobins

(abnormal; electrospray mass spectrometry

permits characterization of **disulfide** bridge-forming human Hb variant Ta-Li (.beta.83Gly.fwdarw.Cys))

IT Disulfide group

Electrospray ionization mass spectrometry Human

Mutation

(electrospray mass spectrometry permits characterization of disulfide bridge-forming human Hb variant Ta-Li (.beta.83Gly.fwdarw.Cys))

IT Quaternary structure

(protein; electrospray mass
spectrometry permits characterization of
disulfide bridge-forming human Hb variant Ta-Li
(.beta.83Gly.fwdarw.Cys))

IT 52-90-4, L-Cysteine, properties

(electrospray mass spectrometry permits characterization of disulfide bridge-forming human Hb variant Ta-Li (.beta.83Gly.fwdarw.Cys))

L102 ANSWER 4 OF 24 HCA COPYRIGHT 2004 ACS on STN
134:337295 Determination of disulfide bond assignments and
N-glycosylation sites of the human gastrointestinal carcinoma
antigen GA733-2 (CO17-1A, EGP, KS1-4, KSA, and Ep-CAM). Chong, Jae
Min; Speicher, David W. (Wistar Institute, Philadelphia, PA, 19104,
USA). Journal of Biological Chemistry, 276(8), 5804-5813 (English)
2001. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society
for Biochemistry and Molecular Biology.

The GA733-2 antigen is a cell surface glycoprotein highly expressed AΒ on most human gastrointestinal carcinoma and at a lower level on most normal epithelia. It is an unusual cell-cell adhesion protein that does not exhibit any obvious relation to the four known classes of adhesion mols. In this study, the disulfide-bonding pattern of the GA733-2 antigen was detd. using matrix-assisted laser desorption/ionization mass spectrometry and N-terminal sequencing of purified tryptic peptides treated with 2-[2'-nitrophenylsulfonyl]-3-methyl-3-bromoindolenine or partially reduced and alkylated. Numbering GA733-2 cysteines sequentially from the N terminus, the first three disulfide linkages are Cys1-Cys4, Cys2-Cys6, and Cys3-Cys5, which is a novel pattern for a cysteine-rich domain instead of the expected epidermal growth factor-like disulfide structure. The next three disulfide linkages are Cys7-Cys8, Cys9-Cys10, and Cys11-Cys12, consistent with the recently detd. disulfide pattern of the thyroglobulin type 1A domain of insulin-like growth factor-binding proteins 1 and Anal. of glycosylation sites showed that GA733-2 antigen contained N-linked carbohydrate but that no O-linked carbohydrate groups were detected. Of the three potential N-linked glycosylation sites, Asn175 was not glycosylated, whereas Asn88 was completely glycosylated, and Asn51 was partially glycosylated. Thus, the extracellular domain of the GA733-2 antigen consists of three distinct domains; a novel cysteine-rich N-terminal domain (GA733 type 1 motif), a cysteine-rich thyroglobulin type 1A domain (GA733 type 2 motif), and a unique nonglycosylated domain without cysteines (GA733 type 3 motif).

CC 6-3 (General Biochemistry)

Section cross-reference(s): 14

- ST gastrointestinal carcinoma antigen GA733 2 **disulfide** bond glycosylation site
- IT Antigens

(17-1A; detn. of **disulfide** bond assignments and N-glycosylation sites of human gastrointestinal carcinoma antigen GA733-2 (CO17-1A, EGP, KS1-4, KSA, and Ep-CAM))

IT Cell adhesion molecules

(Ep-CAM as; detn. of **disulfide** bond assignments and N-glycosylation sites of human gastrointestinal carcinoma antigen GA733-2 (CO17-1A, EGP, KS1-4, KSA, and Ep-CAM))

IT **Digestive** tract

(carcinoma; detn. of **disulfide** bond assignments and N-glycosylation sites of human gastrointestinal carcinoma antigen GA733-2 (CO17-1A, EGP, KS1-4, KSA, and Ep-CAM))

IT Protein motifs

(cysteine-rich N-terminal domain; detn. of disulfide bond assignments and N-glycosylation sites of human gastrointestinal carcinoma antigen GA733-2 (CO17-1A, EGP, KS1-4, KSA, and Ep-CAM))

IT Protein motifs

(cysteine-rich thyroglobulin type 1A domain; detn. of disulfide bond assignments and N-glycosylation sites of human gastrointestinal carcinoma antigen GA733-2 (CO17-1A, EGP, KS1-4, KSA, and Ep-CAM))

IT Disulfide group

(detn. of **disulfide** bond assignments and N-glycosylation sites of human gastrointestinal carcinoma antigen GA733-2 (CO17-1A, EGP, KS1-4, KSA, and Ep-CAM))

IT Protein motifs

(glycosylation site; detn. of **disulfide** bond assignments and N-glycosylation sites of human gastrointestinal carcinoma antigen GA733-2 (CO17-1A, EGP, KS1-4, KSA, and Ep-CAM))

IT Conformation

(loop, protein; detn. of disulfide bond assignments and N-glycosylation sites of human gastrointestinal carcinoma antigen GA733-2 (CO17-1A, EGP, KS1-4, KSA, and Ep-CAM))

IT Protein motifs

(nonglycosylated domain without cysteines; detn. of

disulfide bond assignments and N-glycosylation sites of human gastrointestinal carcinoma antigen GA733-2 (CO17-1A, EGP, KS1-4, KSA, and Ep-CAM))

L102 ANSWER 5 OF 24 HCA COPYRIGHT 2004 ACS on STN
133:346639 Characterization of cysteine residues and
disulfide bonds in proteins by liquid
chromatography/electrospray ionization tandem mass
spectrometry. Yen, Ten-Yang; Joshi, Rajesh K.; Yan, Hui;
Seto, Nina O. L.; Palcic, Monica M.; Macher, Bruce A. (Department of
Chemistry and Biochemistry, San Francisco State University, San
Francisco, CA, 94132, USA). Journal of Mass Spectrometry, 35(8),
990-1002 (English) 2000. CODEN: JMSPFJ. ISSN: 1076-5174.
Publisher: John Wiley & Sons Ltd..

Cvsteine residues and disulfide bonds are AB important for protein structure and function. We have developed a simple and sensitive method for detg. the presence of free cysteine (Cys) residues and disulfide bonded Cys residues in proteins (<100 pmol) by liq. chromatog./electrospray ionization tandem mass spectrometry (LC/ESI-MS/MS) in combination with protein database searching using the program Sequest. Free Cys residues in a protein were labeled with PEO-maleimide biotin immediately followed by denaturation with 8 M urea. Subsequently, the protein was digested with trypsin or chymotrypsin and the resulting products were analyzed by capillary LC/ESI-MS/MS for peptides contq. modified Cys and/or disulfide bonded Cys residues. Although the MS method for identifying disulfide bonds has been routinely employed, methods to prevent thiol-disulfide exchange have not been well documented. Our protocol was found to minimize the occurrence of the thiol-disulfide exchange reaction. The method was validated using well-characterized proteins such as aldolase, ovalbumin, and .beta.-lactoglobulin A. We also applied this method to characterize Cys residues and disulfide bonds of .beta. 1,4-galactosyltransferase (five Cys), and human blood group A and B glycosyltransferases (four Cys). Our results demonstrate that .beta. 1,4-galactosyltransferase contains one free Cys residue and two disulfide bonds, which is in contrast to work previously reported using chem. methods for the characterization of free Cys residues, but is consistent with recently published results from x-ray crystallog. In contrast to the results obtained for .beta. 1,4-galactosyltransferase, none of the Cys residues in A and B glycosyltransferases were found to be involved in disulfide bonds.

IT 52-90-4, Cysteine, analysis (characterization of cysteine residues and disulfide bonds in proteins by liq.

chromatog./electrospray ionization tandem mass
spectrometry)

RN 52-90-4 HCA

CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

CC 9-5 (Biochemical Methods)

Section cross-reference(s): 6, 7

ST cysteine disulfide bond protein electrospray ionization mass spectrometry

IT Digestion, chemical

Disulfide group

Electrospray ionization mass spectrometry Sample preparation

(characterization of **cysteine** residues and **disulfide** bonds in proteins by liq. chromatog./electrospray ionization tandem **mass spectrometry**)

IT Proteins, general, analysis

(characterization of **cysteine** residues and **disulfide** bonds in proteins by liq. chromatog./electrospray ionization tandem **mass spectrometry**)

IT Ovalbumin

(characterization of **cysteine** residues and **disulfide** bonds in proteins by liq. chromatog./electrospray ionization tandem **mass spectrometry**)

IT Liquid chromatography

(coupled with electrospray ionization tandem mass spectrometry; characterization of cysteine residues and disulfide bonds in proteins by liq. chromatog./electrospray ionization tandem mass spectrometry)

IT Mass spectrometry

Mass spectrometry

(liq. chromatog. combined with; characterization of cysteine residues and disulfide bonds in proteins by liq. chromatog./electrospray ionization tandem mass spectrometry)

ΤТ Liquid chromatography Liquid chromatography (mass spectrometry combined with; characterization of cysteine residues and disulfide bonds in proteins by liq. chromatog./electrospray ionization tandem mass spectrometry) ΙT Conformation Denaturation (protein; characterization of cysteine residues and disulfide bonds in proteins by liq. chromatog./electrospray ionization tandem mass spectrometry) ΙT Information systems (searching, computer database; characterization of cysteine residues and disulfide bonds in proteins by liq. chromatog./electrospray ionization tandem mass spectrometry) ΙT Lactoglobulins (.beta.-, A; characterization of cysteine residues and disulfide bonds in proteins by liq. chromatog./electrospray ionization tandem mass spectrometry) 52-90-4, Cysteine, analysis 9024-52-6, Aldolase ΙT 9067-69-0, A-Antigen-forming acetylgalactosaminyltransferase 37257-33-3, Blood group B glycosyltransferase (characterization of cysteine residues and disulfide bonds in proteins by liq. chromatog./electrospray ionization tandem mass spectrometry) 305372-39-8 ΙT 93285-75-7 (characterization of cysteine residues and disulfide bonds in proteins by liq. chromatog./electrospray ionization tandem mass spectrometry) ΙT 9054-94-8 (characterization of cysteine residues and disulfide bonds in proteins by liq. chromatog./electrospray ionization tandem mass spectrometry)

L102 ANSWER 6 OF 24 HCA COPYRIGHT 2004 ACS on STN

133:3553 Mass spectrometric mapping of
 disulfide bonds in recombinant human interleukin-13.
 Tsarbopoulos, Anthony; Varnerin, Jeff; Cannon-Carlson, Susan; Wylie,
 David; Pramanik, Birendra; Tang, John; Nagabhushan, Tattanahalli L.
 (Departments of Bioisolation Process Development and Production,
 Schering-Plough Research Institute, Union, NJ, 07083, USA). Journal

of Mass Spectrometry, 35(3), 446-453 (English) 2000. CODEN: JMSPFJ. ISSN: 1076-5174. Publisher: John Wiley & Sons Ltd.. Interleukin 13 (IL-13), a member of the .alpha.-helical family of AB cytokines, has .apprx.30% primary sequence homol. with IL-4 and shares a common receptor component. The biol. active rhIL-13 is monomeric and non-glycosylated, and contains two disulfide bonds as detd. by comparative electrospray mass spectrometric (MS) anal. of the protein before and after redn. with dithiothreitoldithioerythritol. A trypsin-resistant core peptide of rhIL-13 was isolated and analyzed by plasma desorption (PD) MS, identifying a disulfide-linked core peptide. Subsequent digestion of this core peptide by pepsin, followed by PDMS anal. of the resulting cystine-contg. peptic fragments, provided rapid detn. of the existing disulfide bonds between cysteine residues 28-56 and 44-70. This disulfide arrangement is similar to that obsd. for the analogous four internal cysteine residues in hIL-4. The conservation of disulfide bond arrangements between hIL-13 and hIL-4, coupled with their .alpha.-helical structure and sequence homologies, confirms that IL-13 and IL-4 are structural homologs. It is also consistent with their reported similarities in biol. function and receptor binding kinetics. 15-5 (Immunochemistry)

CC

disulfide bond interleukin 13 ST

Interleukin 13 ΙT

(disulfide linkage assignment in recombinant human IL-13

Disulfide group ΙT

(linkage assignment in recombinant human interleukin-13)

L102 ANSWER 17 OF 24 HCA COPYRIGHT 2004 ACS on STN 125:81167 S-Pyridylethylation of intact polyacrylamide gels and in situ digestion of electrophoretically separated proteins: a rapid mass spectrometric method for identifying cysteine-containing peptides. Moritz, Robert L.; Eddes, James S.; Reid, Gavin E.; Simpson, Richard J. (Ludwig Inst. Cancer Res., Walter Eliza Hall Inst. Med. Res., Parkville, Australia). Electrophoresis, 17(5), 907-917 (English) 1996. CODEN: ELCTDN. ISSN: 0173-0835. Publisher: VCH. In-gel proteolytic digestion of acrylamide-gel sepd. AΒ proteins is a method widely used for generating peptide fragments for the purpose of identifying proteins

by Edman degrdn., tandem mass spectrometry, and peptide-mass fingerprinting. However, it is well recognized for disulfide-bonded proteins electrophoresed under reducing conditions that if no precautions are taken to

minimize disulfide bond formation during protein digestion or peptide isolation, complex peptide maps can result. Here, we describe an improved method for in-gel protein digestion. It consists of first reducing and S-pyridylethylating Coomassie Brilliant Blue R-250-stained proteins immobilized in the whole-gel slab with dithiothreitol and 4-vinylpyridine, excising the individual stained and alkylated proteins, an then digesting them in situ in the gel matrix with trypsin or Achromobacter lyticus protease I. Peptide fragments generated in this manner are extd. from the gel piece and purified to homogeneity by a rapid (.ltoreq.12 min) reversed-phase high performance lig. chromatog. (HPLC) procedure, based upon conventional silica supports. Recoveries of peptides are increased by S-pyridylethylation of acrylamide-immobilized proteins prior to in-gel digestion. Further, the levels of gel-related contaminants, which otherwise result in suppression of sample signals during electrospray ionization mass spectrometry, are greatly reduced by the redn./alkylation step. Addnl., we demonstrate the S-.beta.-(4-pyridylethyl)-cysteine contg. peptides can be readily identified during reversed-phase HPLC by absorbance at 254 nm, and during electrospray ionization tandem mass spectrometry by the appearance of a characteristicpyridylethyl fragment ion of 106 Da. The position of cysteine residues in a sequence can be detd. as phenylthiohydantoin S-.beta.-(4-pyridylethyl)-cysteine during Edman degrdn., and by tandem mass spectrometry.

- CC 9-16 (Biochemical Methods)
- ST pyridylethylation polyacrylamide gel digestion electrophoresis; protein mass spectrometry cysteine peptide
- IT Edman degradation

(S-Pyridylethylation of intact polyacrylamide gels and in situ digestion of electrophoretically sepd. proteins: a rapid mass spectrometric method for identifying cysteine-contg. peptides)

IT Peptides, analysis

(cysteine-contg., S-Pyridylethylation of intact polyacrylamide gels and in situ digestion of electrophoretically sepd. proteins: a rapid mass spectrometric method for identifying cysteine -contg. peptides)

IT Mass spectrometry

(tandem, S-Pyridylethylation of intact polyacrylamide gels and in situ digestion of electrophoretically sepd. proteins: a rapid mass spectrometric method for identifying cysteine-contg. peptides)

IT 100-43-6, 4-Vinylpyridine 3483-12-3, Dithiothreitol (S-Pyridylethylation of intact polyacrylamide gels and in situ digestion of electrophoretically sepd. proteins: a rapid mass spectrometric method for identifying cysteine-contg. peptides)

L102 ANSWER 22 OF 24 HCA COPYRIGHT 2004 ACS on STN

114:58326 Strategies for determination of disulfide bridges in proteins using plasma desorption mass spectrometry

. Soerensen, Hans Holmegaard; Thomsen, Johannes; Bayne, Stephen; Hoejrup, Peter; Roepstorff, Peter (Novo Nordisk A/S, Gentofte, DK-2820, Den.). Biomedical & Environmental Mass Spectrometry, 19(11), 713-20 (English) 1990. CODEN: BEMSEN. ISSN: 0887-6134.

- AΒ Disulfide bridges have been assigned in 3 different proteins by locating possible disulfide-linked peptides in enzymic digests of the proteins based on their mol. wt. detd. by plasma desorption mass spectrometry. Different strategies have been employed including in situ redn. of the nitrocellulose-bound peptides and confirmation of peptide identify by Me esterification reactions or Edman degrdn. The latter was needed for identification of glycosylated disulfide-linked peptides. For insulins cleavaged between cysteine residues in close proximity was not possible; but a combination of mol. mass information, enzymic cleavage with 2 different enzymes and sequence anal. including identification of diphenylthiohydantoin-cystine could ensure an unambiguous assignment of the disulfide bridges.
- CC 9-5 (Biochemical Methods)
 Section cross-reference(s): 6
- ST disulfide group detn protein
 mass spectrometry; plasma desorption mass
 spectrometry protein disulfide
- IT Disulfide group

(detn. of, in proteins by plasma desorption mass spectrometry, strategies for)

IT Glycoproteins, analysis

(disulfide bridges detn. in, by plasma desorption mass spectrometry, strategies for)

IT Proteins, specific or class

(15,000-mol.-wt., disulfide bridges detn. in, by plasma desorption mass spectrometry, strategies for)

IT Proteins, specific or class

(disulfide-contg., disulfide bridges detn. in, by plasma desorption mass spectrometry, strategies for)

IT Mass spectroscopy

(plasma-desorption, disulfide bridges in